FY 1999 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

FY 1999 marked the seventh year of statutorily specified performance under the original Prescription Drug User Fee Act (PDUFA) of 1992 and the second year under the expanded performance specifications set forth in the Food and Drug Administration Modernization Act (FDAMA) of 1997. The FY 1999 performance requirements continued the multi-year progression toward ever shorter review time goals and added a number of new performance goals that required new tracking and management capabilities within FDA.

In FY 1999, FDA reviewed and acted upon a total of 2,111 PDUFA-related original and resubmitted new product applications, original efficacy supplements, and original manufacturing supplements. This workload increased more than 12 percent over the 1,899 PDUFA-related review decisions the Agency made in FY 1998. More than 98 percent of the decisions made in FY 1999 were within the prescribed PDUFA time frames.

In addition, FY 1999 posted the first year of FDA performance on a variety of new goals seeking to shorten the investigative phase of drug development. In FY 1999 FDA took action on a total of 4,062 goal-specific events relating to sponsor meetings and other drug development milestones. The vast majority of these actions had no performance goals prior to FY 1999.

Despite the increased workload, the more numerous goals, and the shorter target review times, the high level of performance that FDA has achieved under PDUFA continued in FY 1999.

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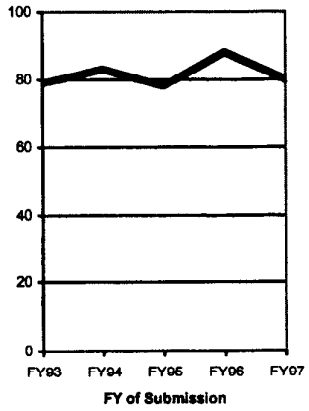
Outcomes

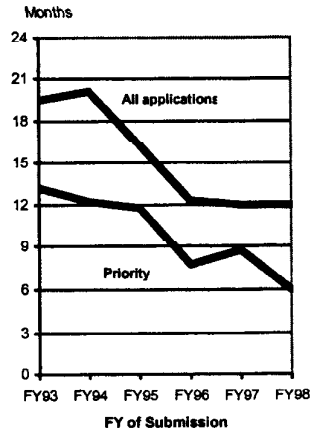
The last two PDUFA Performance Reports identified several important outcomes that had resulted from the Agency's meeting and exceeding its application review performance commitments. These included increasing numbers of applications filed, higher quality applications, and quicker approvals for products with the requisite data; outcomes that result in more quality products reaching American practitioners and consumers faster. While the Agency continues to exceed the review performance goals of PDUFA II[1] even as the goals become more challenging each year, the rapid gains of the early PDUFA years have slowed. Still, application filings and quality remain high by historic standards, and approval times continue to drop.

Percent of Applications Approved



High Approval Rates: The percentage of filed new product applications that ultimately are approved increased from the less than 60% rate of the pre-PDUFA years[2] to roughly 80% for applications submitted from FY 93 through FY 95. These early PDUFA cohorts are essentially finished; no submissions from earlier than FY 96 were approved in FY 99. The approval rate for FY 96 new product applications currently stands at 88% and could reach 90% if the sponsors are able to submit adequate answers to noted deficiencies. For the FY 97 applications, 97 of 133 (73%) have been approved, and the final approval rate should be above 80% if present trends hold.

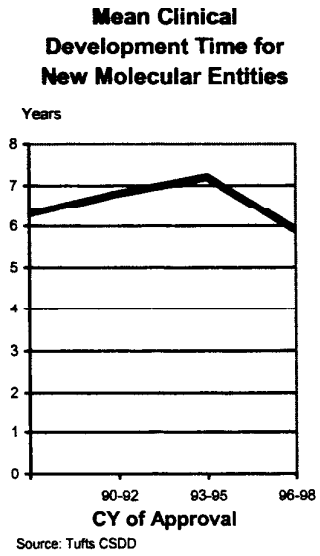
Median Approval Times



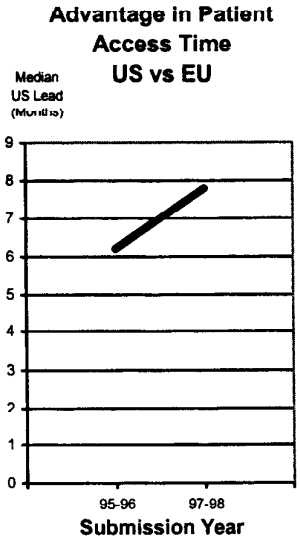
Quick Approval Times: The median total approval time for new product applications submitted in FY 98 was 12 months[3], as it was for FY 96 and FY 97 submissions. Total approval time is the time from the initial submission of a marketing application to the issuance of an approval letter for that application. It includes both FDA's review time and the time the sponsor spends answering deficiencies noted by FDA and can encompass several review 'cycles.' Given the progression of PDUFA II review goals, median approval times may drop to 10 months in FY 2001 or FY 2002 if the current rate of first review cycle approvals is sustained.

Median total approval times for priority applications submitted in FY 98 dropped to 6 months[3], less than half the median approval times for priority applications submitted in the early PDUFA years. The products of priority applications represent significant therapeutic gains and are an important outcome for the consumer and the medical community.

Shorter Drug Development Times: The time consumed by the clinical development phase of drug development has decreased by 18% in recent years. An independent study by the Tufts Center for the Study of Drug Development[4] reports that new molecular entities approved from 1996-98 required an average of only 5.9 years of clinical research compared with 7.2 years for the preceding 1993-95 interval. This 15-month savings in overall drug development time coincides with the substantial PDUFA I increase in FDA/Sponsor interactions regarding the clinical trial process. Additional savings are expected in future years as the PDUFA II goals regarding FDA/Sponsor meetings are realized.



Comparative International Timeliness: The United States was, once again in 1999, the decisive leader in first world introductions of new pharmaceutical therapies. Direct comparison of the European Union's (EU) regulatory approval system with FDA through the 1998 submission year demonstrates a sustained and significant U.S. patient availability advantage for new molecular entities of more than six months.



REPORT ON PDUFA GOALS

This report updates the Agency's review performance on the FY 98 application submissions and evaluates its performance in reviewing FY 99 application submissions and meeting other PDUFA II goals. All but one of the FY 98 submissions have been reviewed and acted upon, and final performance relative to the goals can now be reported. Only a preliminary performance assessment on FY 99 submissions 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, 1999.

This report continues the reporting conventions first described in the FY 1998 report:

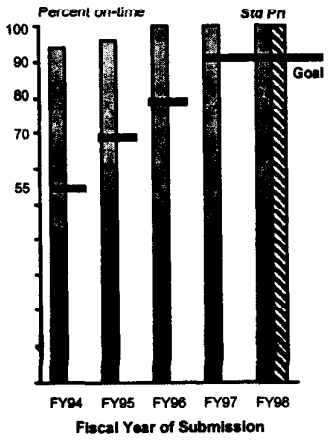
- Although many of the Agency's performance goals under PDUFA II are new and have no parallels under PDUFA I, the goals relating directly to application review seek to extend and improve on the gains made under PDUFA I. This report continues to show both current performance and past performance relative to these review goals. The report shows performance for the last five years.
- CBER is in the process of changing from counting PLAs and ELAs separately to combining them as BLAs (Biologic License Applications). 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.
- In earlier PDUFA Performance Reports, the "Workload" and "Performance" figures for NDAs excluded original new product applications that fell under the PDUFA definition of "human drug products" but which did not pay fees. Since these applications are subject to the same performance goals as the fee-paying applications, they are included in this report, both under "Workload" and in the "Performance" figures. Workload figures from earlier years have been adjusted to include these applications also.

Original New Product Applications

Goal --Review and act upon complete NDAs and BLAs[5]

On-time Goal		Submission Year				
		FY 98	FY 99	FY 00	FY 01	FY 02
Priority	6 months	90%	90	90	90	90
Standard	12 months	90%	90	90	90	
	10 months		30	50	70	90

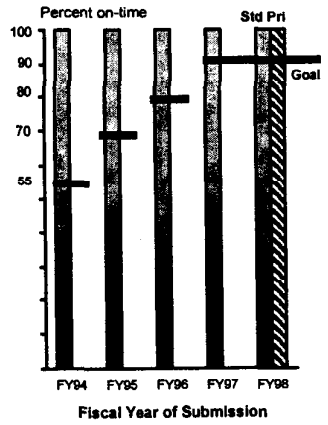
NDAs



Workload -- Original submissions filed *(Priority/Standard)*:

	FY 95	FY 96	FY 97	FY 98	FY 99[6]
• **NDAs**	109	106	117 *(25/92)*	108 *(30/78)*	121 *(29/92)*
• **BLAs**	12	9	16 *(3/13)*	12 *(8/4)*	6 *(1/5)*
• **PDUFA Total**	121	115	133 *(28/105)*	120 *(38/82)*	127 *(30/97)*
NMEs[7]				43 *(19/24)*	43 *(16/27)*

BLAs



Performance

FY 98 Submissions:

- All 120 FY 98 submissions have been reviewed and acted upon, all on time.

FY 99 Submissions:

- All 26 (19 priority and 7 standard) FY 99 submissions that have been reviewed and acted upon were on time.
- Early indicator performance for 18 priority (6-month goal) NDAs received during the first six months of FY 99 is 100 percent on time. No priority BLAs were received in the first 6 months.

NMEs and BLAs

- All 43 discrete NMEs (19 priority and 24 standard) and 12 BLAs (8 priority and 4 standard) submitted in FY 98 have been reviewed and acted upon, all on time. All 10 priority NMEs received in the first 6 months of FY 99 were reviewed and acted upon on time.

Resubmitted New Product Applications

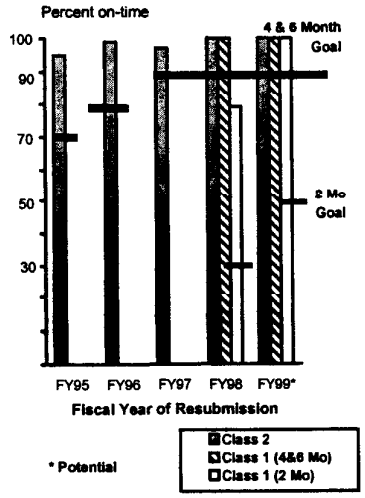
Goal – **Review and act upon resubmitted[8] NDAs and BLAs[5]**

On-time Goal		Resubmission Year				
		FY 98	FY 99	FY 00	FY 01	FY 02
Class 1	6 months	90				
	4 months		90	90		
	2 months	30	50	70	90	90
Class 2	6 months	90	90	90	90	90

Workload – **Resubmissions received** [Total (*Class 1/Class 2*)]

	FY95	FY96	FY97	FY 98	FY 99
• **of Original NDAs**	58	84	82	49 *(19/30)*	59 *(20/39)*
• **of Original BLAs**	3	14	8	21 *(5/16)*	14 *(2/12)*
• **PDUFA Total**	61	98	90	70 *(24/46)*	73 *(22/51)*

Resubmitted NDAs



Performance

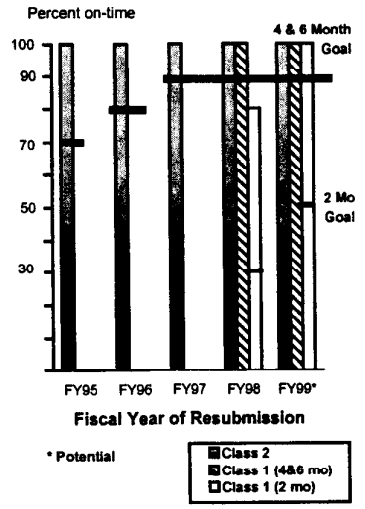
FY 98 Resubmissions:

- 79 percent (19 of 24) of all Class 1 resubmissions were reviewed and acted upon within 2 months; all were reviewed and acted upon within 6 months.
- All 46 of the Class 2 resubmissions were reviewed and acted upon within 6 months.

FY 99 Resubmissions:

- All 17 of the Class 1 resubmissions that have been reviewed and acted upon have met the 2-month review goal.
- All 27 of the Class 2 resubmissions that have been reviewed and acted upon have met the 6-month review goal.
- Early-indicator performance for 17 Class 1 resubmissions submitted in the first 10 months of FY 99 is 100% reviewed and acted upon within 2 months.
- Early-indicator performance for 19 Class 2 resubmissions submitted in the first 6 months of FY 99 is 100% on time (i.e., within 6 months).

Resubmitted BLAs

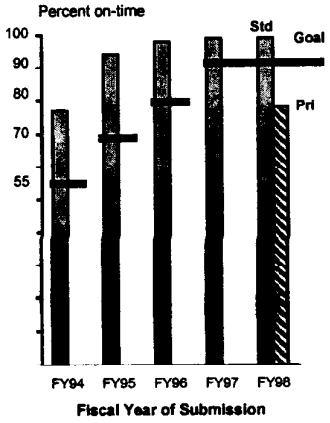


Efficacy Supplements

Goal – Review and act upon complete efficacy supplements to NDAs and BLAs[5]

On-time Goal		Submission Year				
		FY 98	FY 99	FY 00	FY 01	FY 02
Priority	6 months	90%	90	90	90	90
Standard	12 months	90%	90	90	90	
	10 months		30	50	70	90

NDA Efficacy Supplements



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

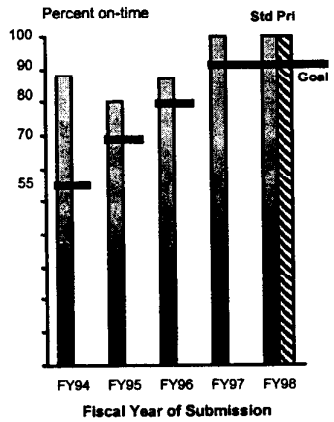
	FY 95	FY 96	FY 97	FY 98	FY 99[6]
• **to NDAs**	77	103	146 *(10/136)*	128 *(9/119)*	138 *(16/122)*
• **to BLAs**	10	8	15 *(3/12)*	10 *(1/9)*	9 (2/7)
• **PDUFA total**	87	111	161 *(13/148)*	138 *(10/128)*	147 *(18/129)*

Performance

FY 98 Submissions:

- 8 of 10 priority efficacy supplements were reviewed and acted upon on time. Combined CDER/CBER performance was 80 percent on time.
- All but one of the 128 standard efficacy supplements have been reviewed and acted upon, all on time. The one that has not been reviewed is overdue. Combined CDER/CBER performance was 99 percent on time.

BLA Efficacy Supplements



FY 99 Submissions:

- As of September 30, 1999, 7 priority and 22 standard FY 99 efficacy supplements had been reviewed and acted upon. All the standard supplements and 6 of the priorities were on time.
- Combined CDER/CBER early-indicator performance for 7 priority efficacy supplements (6-month goal) received during the first 6 months of FY 99 is 86 percent on time.

Goal – Review and act upon complete manufacturing supplements to NDAs and BLAs[5]

Manufacturing Supplements

On-time Goal		Submission Year				
		FY 98	FY 99	FY 00	FY 01	FY 02
Prior approval not required	6 months	90%	90	90	90	90
Prior approval required	6 months	90%	90	90	90	
	4 months		30	50	70	90

Workload -- Manufacturing supplements filed *(Total/Prior App)*:

	FY 95	FY 96	FY 97	FY 98	FY 99[6]
• **to NDAs**	1,249	1,218	1,262	1,463	1,468 *(994)*
• **to BLAs**	273	261	338	371	390 *(251)*
• **PDUFA total**	1,522	1,479	1,600	1,834	1,858 *(1,245)*

Performance:

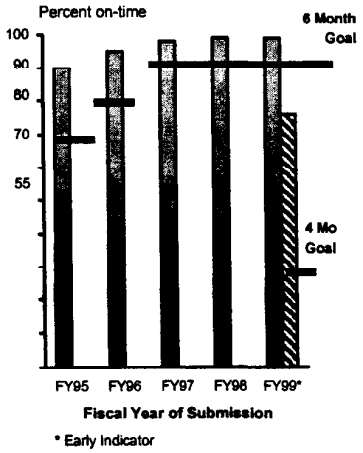
FY 98 Submissions:

- All 1,834 FY 98 manufacturing supplements have been reviewed and acted upon, 1,807 on time.
- *Combined CDER/CBER on-time performance was 99 percent.*

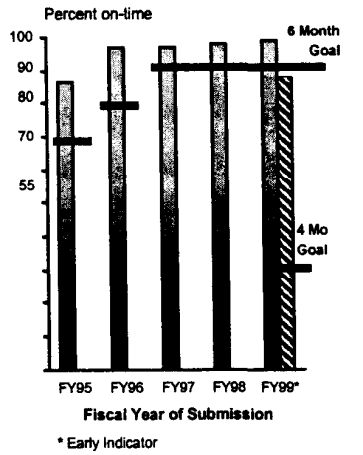
FY 99 Submissions:

- 1,148 FY 99 manufacturing supplements have been reviewed and acted upon; 758 were prior approval supplements.
- 99 percent of all manufacturing supplements reviewed and acted upon were within the 6-month goal and 80 percent of the prior approval supplements reviewed and acted upon were within the 4-month goal.
- Early indicator performance on all 864 manufacturing supplements received in the first 6 months of FY 99 is 99 percent on time.
- Early indicator performance on the 720 prior approval supplements (4 month goal) received in the first 8 months of FY 99 is 78 percent on time.

NDA Manufacturing Supplements



BLA Manufacturing Supplements



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 B. This section reports on actions on items that occurred in FY 99.

Meeting Management:

- **Meeting Requests:** Notify requestor of formal meeting in writing within 14 days of request.
- **Scheduling Meetings:** Schedule meetings within goal date or within 14 days of requested date if longer than 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.
- **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	Pending[9]	% On Time[10]
On time Goal							**70%**
Meeting Requests		CBER	381	274	105	2	
		CDER	1163	1049	84	30	
		Combined	1544	1323	189	32	**88%**
Scheduling Meetings	Type A	CBER	22	16	3	3	
		CDER	27	17	8	2	
	Type B	CBER	284	215	30	39	
		CDER	504	366	120	18	
	Type C	CBER	53	50	1	2	
		CDER	578	548	19	11	
	All	CBER	359	281	34	44	
		CDER	1109	931	147	31	
		Combined	1468	1212	181	75	**87%**
Meeting Minutes		CBER	290	226	34	30	
		CDER	1045	575	133	337	
		Combined	1335	801	167	367	**83%**

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	Pending Within Goal	% On Time[10]
On-time Goal					**90%**
CBER	75	67	4	4	
CDER	49	40	5	4	
Combined	124	107	9	8	**92%**

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

	Total	Met Goal	Missed Goal	Pending Within Goal	% On Time[10]
On-time Goal					**70%**
CBER	1	1	0	0	
CDER	6	4	2	0	
Combined	7	5	2	0	**71%**

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	Pending Within Goal	% On Time[10]
On-time Goal					**60%**
CBER	0	0	0	0	•
CDER	69	64	2	3	
Combined	69	64	2	3	**97%**

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] Source: United States General Accounting Office, FDA Drug Approval: Review Time Has Decreased in Recent Years (GAO/PEMD-96-1), October 1995

[3] Although the last approvals for FY 98 submissions (as well as for earlier years) have not yet occurred, the median statistic can be computed from approvals to date and estimates of the percent of submissions that will ultimately be approved.

[4] Tufts Center for the Study of Drug Development Impact Report, "Clinical development times for new drugs drop 18%, reversing 12-yr trend", http://www.tufts.edu/med/research/csdd, (Volume 1, July 1999)

[5] CBER's workload counts and performance statistics in PDUFA I Performance Reports included original and resubmitted ELAs. CBER is in the process of changing from counting PLAs and ELAs separately to combining them as BLAs (Biologic License Applications). This report shows CBER's workload and performance on PLAs and BLAs only (i.e., Product Applications) and, for notational simplicity, refers to both as BLAs. Original and resubmitted ELAs have been dropped, both from workload counts and performance measurements.

[6] The count of FY 99 submissions assumes that all submissions received in the last two months of FY 99 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.

[7] 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 re-designated as non-NMEs. In FY 99, CDER designated 47 filings as NMEs initially (16 priority, 31 standard). Only 43 of these are 'discrete' (16 priority, 27 standard).

[8] 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 its original application's year of submission.

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

[10] Actions pending were excluded from the calculation.

APPENDIX A: PURPOSE

The Prescription Drug User Fee Act of 1992, Public Law 102-571, authorized revenues from fees paid by the pharmaceutical industry to expedite review by the Food and Drug Administration (FDA) of human drug applications. The Food and Drug Administration Modernization Act of 1997 (FDAMA), Public Law 105-115, extended this authorization until FY 2002. Along with the extension of revenues, the FDA agreed to meet increasingly stringent review time frames and other procedural performance goals.

FDAMA 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 1999.

APPENDIX B: PDUFA PERFORMANCE GOALS, FY 1998 - FY 2002

The following list presents by fiscal year the performance measures set forth in the letters referenced in the Food and Drug Administration Modernization Act of 1997. The following chart lists the goals by fiscal year with appropriate goal measurement dates:

I. FIVE-YEAR REVIEW PERFORMANCE GOALS	MEASUREMENT DATE
Fiscal Year 1998	
1. Review and act on 90 percent of standard original NDAs and PLA/BLAs filed during FY 98 within 12 months of receipt.[1]	12 months after end of FY 1998
2. Review and act on 90 percent of priority original NDAs and PLA/BLAs filed during FY 98 within 6 months of receipt.[1]	6 months after end of FY 1998
3. Review and act on 90 percent of standard efficacy supplements filed during FY 98 within 12 months of receipt.	12 months after end of FY 1998
4. Review and act on 90 percent of priority efficacy supplements filed during FY 98 within 6 months of receipt.	6 months after end of FY 1998
5. Review and act on 90 percent of manufacturing supplements filed during FY 98 within 6 months of receipt.	6 months after end of FY 1998
6. Review and act on 90 percent of resubmitted original applications received during FY 98 within 6 months of receipt, and review and act on 30 percent of Class 1 resubmitted original applications within 2 months of receipt.	6 months after end of FY 1998

[1] The statute allows three additional months for review of original NDA, PLA, or BLA submissions that involve major amendments within the last three months of their usual review interval. In these cases, the measurement dates shown in this Appendix move forward by 3 months.

Fiscal Year 1999

1. Review and act on 90 percent of standard original NDAs and PLA/BLAs filed during FY 99 within 12 months of receipt and review and act on 30 percent within 10 months of receipt.[1]	12 months after end of FY 99
2. Review and act on 90 percent of priority original NDAs and PLA/BLAs filed during FY 99 within 6 months of receipt.[1]	6 months after end of FY 99
3. Review and act on 90 percent of standard efficacy supplements filed during FY 99 within 12 months of receipt and review and act on 30 percent within 10 months of receipt.	12 months after end of FY 99
4. Review and act on 90 percent of priority efficacy supplements filed during FY 99 within 6 months of receipt.	6 months after end of FY 99
5. Review and act on 90 percent of manufacturing supplements filed during FY 99 within 6 months of receipt and review and act on 30 percent of manufacturing supplements requiring prior approval within 4 months of receipt.	6 months after end of FY 99
6. Review and act on 90 percent of Class 1 resubmitted original applications received during FY 99 within 4 months of receipt, and review and act on 50 percent within 2 months of receipt.	4 months after end of FY 99
7. Review and act on 90 percent of Class 2 resubmitted original applications received during FY 99 within 6 months of receipt.	6 months after end of FY 99

Fiscal Year 2000

1. Review and act on 90 percent of standard original NDAs and PLA/BLAs filed during FY 2000 within 12 months of receipt and review and act on 50 percent within 10 months of receipt.[1]	12 months after end of FY 2000
2. Review and act on 90 percent of priority original NDAs and PLA/BLAs filed during FY 2000 within 6 months of receipt.[1]	6 months after end of FY 2000
3. Review and act on 90 percent of standard efficacy supplements filed during FY 2000 within 12 months of receipt and review and act on 50 percent within 10 months of receipt.	12 months after end of FY 2000
4. Review and act on 90 percent of priority efficacy supplements filed during FY 2000 within 6 months of receipt.	6 months after end of FY 2000
5. Review and act on 90 percent of manufacturing supplements filed during FY 2000 within 6 months of receipt and review and act on 50 percent of manufacturing supplements requiring prior approval within 4 months of receipt.	6 months after end of FY 2000
6. Review and act on 90 percent of Class 1 resubmitted original applications received during FY 2000 within 4 months of receipt, and review and act on 70 percent within 2 months of receipt.	4 months after end of FY 2000
7. Review and act on 90 percent of Class 2 resubmitted original applications received during FY 2000 within 6 months of receipt.	6 months after end of FY 2000

Fiscal Year 2001	
1. Review and act on 90 percent of standard original NDAs and PLA/BLAs filed during FY 2001 within 12 months of receipt and review and act on 70 percent within 10 months of receipt.[1]	12 months after end of FY 2001
2. Review and act on 90 percent of priority original NDAs and PLA/BLAs filed during FY 2001 within 6 months of receipt.[1]	6 months after end of FY 2001
3. Review and act on 90 percent of standard efficacy supplements filed during FY 2001 within 12 months of receipt and review and act on 70 percent within 10 months of receipt.	12 months after end of FY 2001
4. *Review and act on 90 percent of priority efficacy supplements filed during FY 2001* within 6 months of receipt.	*6 months after end of* FY 2001
5. Review and act on 90 percent of manufacturing supplements filed during FY 2001 within 6 months of receipt and review and act on 70 percent of manufacturing supplements requiring prior approval within 4 months of receipt.	6 months after end of FY 2001
6. Review and act on 90 percent of Class 1 resubmitted original applications received during FY 2001 within 2 months of receipt.	2 months after end of FY 2001
7. Review and act on 90 percent of Class 2 resubmitted original applications received during FY 2001 within 6 months of receipt.	6 months after end of FY 2001

Fiscal Year 2002	
1. Review and act on 90 percent of standard original NDAs and PLA/BLAs filed during FY 2002 within 10 months of receipt.[1]	12 months after end of FY 2001
2. Review and act on 90 percent of priority original NDAs and PLA/BLAs filed during FY 2002 within 6 months of receipt.[1]	6 months after end of FY 2001
3. Review and act on 90 percent of standard efficacy supplements filed during FY 2002 within 10 months of receipt.	12 months after end of FY 2001
4. Review and act on 90 percent of priority efficacy supplements filed during FY 2001 within 6 months of receipt.	6 months after end of FY 2001
5. Review and act on 90 percent of manufacturing supplements filed during FY 2001 within 6 months of receipt and review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt.	6 months after end of FY 2001
6. Review and act on 90 percent of Class 1 resubmitted original applications received during FY 2001 within 2 months of receipt.	2 months after end of FY 2001
7. Review and act on 90 percent of Class 2 resubmitted original applications received during FY 2001 within 6 months of receipt.	6 months after end of FY 2001

II. NEW MOLECULAR ENTITY (NME) PERFORMANCE GOALS

The performance goals for standard and priority original NMEs will be the same as for all of the original NDAs but will be reported separately.

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

III. PROCEDURAL AND PROCESSING GOALS

Performance Area	Agency Activity	Performance Goal	Performance Level
Meeting Management	Meeting Requests – Notify requestor of formal meeting in writing (date, time, place, and participants)	within 14 days of receipt of request	FY 1999 requests – 70% on time FY 2000 – 80% on time FY2001 and on – 90% on time
	Scheduling Meetings – Schedule meetings within goal date or within 14 days of requested date if longer than goal date.	Type A Meetings within 30 days of receipt of request Type B Meetings within 60 days of receipt of request Type C Meetings within 75 days of receipt of request	FY 1999 requests – 70% on time FY 2000 – 80% on time FY2001 and on – 90% on time
	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	FY 1999 meetings – 70% on time FY 2000 – 80% on time FY2001 and on – 90% on time
Clinical Holds	Response to sponsor's complete response to a clinical hold	within 30 days of receipt of sponsor's response	FY 1998 – 75% on time FY 1999 and on – 90% on time
Major Dispute Resolution	Response to sponsor's appeal of decision	within 30 days of receipt of sponsor's appeal	FY 1999 – 70% on time FY 2000 – 80 % on time FY 2001 and on – 90% on time
Special Protocol Question Assessment and Agreement	Response to sponsor's request for evaluation of protocol design	within 45 days of receipt of protocol and questions	FY 1999 – 60% on time FY 2000 – 70% on time FY 2001 – 80% on time FY 2002 – 90% on time
Electronic Applications and Submissions	Paperless Application Processing	Agency to develop and update information systems to allow paperless receipt and processing of INDs, human drug applications, and related submissions by end of FY 2002.	
Additional Procedures	Simplification of Action Letters	Centers to amend regulations and processes to provide for issuance of 'Approval' (AP) or 'Complete Response' (CR) action letters.	
	Sponsor Notification of Deficiencies in Applications	Centers to notify sponsors of deficiencies via 'information request' (IR) when each discipline has finished its initial review.	

Definitions of Terms:

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

B. A major amendment to an original application submitted within three months of the goal date extends the goal date by three months. Only one extension is allowed for an application.

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

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

1. Final printed labeling
2. Draft labeling
3. Safety updates submitted in the same format, including tabulations, as the original safety submission with new data and changes highlighted (except when large amounts of new information including important new adverse experiences not previously reported with the product are presented in the resubmission)
4. Stability updates to support provisional or final dating periods
5. Commitments to perform Phase 4 studies, including proposals for such studies
6. Assay validation data
7. Final release testing on the last 1-2 lots used to support approval
8. A minor reanalysis of data previously submitted to the application (determined by the agency as fitting the Class 1 category)
9. Other minor clarifying information (determined by the Agency as fitting the Class 1 category)
10. Other specific items may be added later as the Agency gains experience with the scheme and will be communicated via guidance documents to industry.

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

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

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

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

APPENDIX C: LIST OF APPROVED APPLICATIONS

This appendix updates the detailed review histories of the NDAs and PLA/BLAs submitted and approved under PDUFA. It shows approvals of all PDUFA-related submissions that took place in FY 99 as well as FY 98 approvals of FY 98 submissions. Earlier PDUFA approvals were listed in previous performance reports.

The following two tables summarize the review histories for all approved applications submitted from FY 93 through FY 98. The tables show the average first review, second review, and approval times. Note that times are in months, not all applications required a second review, and some required more than two reviews. The mean total approval times shown in the tables will increase in the future as additional applications are approved.

Approved Priority NDAs/BLAs

	1st Review		2nd Review			Total
Receipt Cohort	N	FDA Review	n	Sponsor Response	FDA Review	Approval Time
FY93	13	9.8	5	5.1	3.0	14.2
FY94	13	9.8	8	1.6	3.4	12.9
FY95	21	8.7	10	6.0	3.3	13.2
FY96	31	7.5	13	3.1	3.7	12.1
FY97	23	6.3	10	4.4	3.6	9.5
FY98	29	6.1	11	1.3	2.4	7.5

Approved Standard NDAs/BLAs

	1st Review		2nd Review			Total
Receipt Cohort	n	FDA Review	n	Sponsor Response	FDA Review	Approval Time
FY93	59	15.0	42	5.5	4.7	25.7
FY94	65	12.7	50	5.3	4.4	22.9
FY95	82	12.2	52	2.8	4.2	17.3
FY96	70	11.9	37	3.4	4.0	16.0
FY97	74	11.5	27	2.4	3.1	13.6
FY98	31	11.3	7	2.1	3.8	12.7

The remainder of this appendix shows the individual review histories. Approvals are grouped by submission year and priority designation and listed in order of total approval time. Review histories of all other PDUFA submissions approved prior to FY 98 can be found in the appendices of the earlier PDUFA Performance Reports which are available at http://www.fda.gov.

TERMS AND CODING USED IN TABLES

✓	FY 98 approval of an FY 98 submission. These were not included in earlier PDUFA performance reports and are included here for completeness.
**	Major amendment was received within 3 months of the action due date, which extended the review timeframes by 3 months.
Action Codes:	AE = Approvable AP = Approved NA = Not Approvable RL = Complete Response WD = Withdrawn

Table 1

FY 1998 Priority NDA and BLA Submissions Approved in FY 98 (✓) and FY 99

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
✓ EFAVIRENZ	Dupont Pharms	3.2		Y
✓ FOMIVIRSEN SODIUM	Ciba Vision	4.6		Y
✓ TRASTUZUMAB (BLA)	Genentech, Inc.	4.7		Y
✓ NEVIRAPINE	Boehringer Pharms	4.7		Y
ETANERCEPT (BLA)	Immunex Corporation	5.8		Y
ABACAVIR SULFATE (TABLET)	Glaxo Wellcome	5.8		Y
ABACAVIR SULFATE (ORAL SOLUTION)	Glaxo Wellcome	5.8		Y
OCTREOTIDE ACETATE	Novartis Pharms	5.9		Y
✓ RIBAVIRIN	Schering Plough Res	5.9		Y
✓ BASILIXIMAB (BLA)	Novartis Pharmaceutical Corporation	6.0		Y
✓ PALIVIZUMAB (BLA)	MedImmune, Inc	6.0		Y
✓ CAPECITABINE	HLR	6.0		Y
✓ RIFAPENTINE	Hoechst Marion Rssl	6.0		Y
✓ LEFLUNOMIDE	Hoechst Marion Rssl	6.0		Y
BUSULFAN	Orphan Medcl	6.0		Y
CELECOXIB	Searle	6.0		Y
✓ TIROFIBAN HYDROCHLORIDE .05MG/ML	Merck Res	6.4	FDA First Action: 6.0 (AE) Sponsor Response: 0.2 FDA Second Action: 0.3 (AP)	Y Y
✓ TIROFIBAN HYDROCHLORIDE .25MG/ML	Merck Res	6.4	FDA First Action: 6.0 (AE) Sponsor Response: 0.2 FDA Second Action: 0.3 (AP)	Y Y
HEPATITIS B IMMUNE GLOBULIN (HUMAN) (PLA)	Nabi	7.3	FDA First Action: 5.6 (RL) Sponsor Response: 0.2 FDA Second Action: 1.5 (AP)	Y Y
✓ INFLIXIMAB (BLA)	Centocor, Inc.	7.8	FDA First Action: 6.0 (RL) Sponsor Response: 1.2 FDA Second Action: 0.6 (AP)	Y Y
MIDAZOLAM HYDROCHLORIDE	Roche	8.2	FDA First Action: 5.9 (AE) Sponsor Response: 2.0 FDA Second Action: 0.3 (AP)	Y Y

Table 1 (continued)

	Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
			Total Time	Resubmissions (if necessary)	
	ALITRETINOIN	Ligand	8.3	FDA First Action: 6.0 (AE)	Y
				Sponsor Response: 0.3	
				FDA Second Action: 2.0 (AP)	Y
✓	VALRUBICIN	Anthra	8.8		Y**
✓	GLUCAGON	Lilly	9.0		Y**
✓	LEVONORGESTREL/ ETHINYL ESTRADIOL	Gynetics	9.0		Y**
	THYROTROPIN ALFA	Genzyme Fine	11.5	FDA First Action: 9.0 (AE)	Y**
				Sponsor Response: 0.8	
				FDA Second Action: 1.7 (AP)	Y
	TEMOZOLOMIDE	Schering	11.9	FDA First Action: 6.0 (AE)	Y
				Sponsor Response: 4.4	
				FDA Second Action: 1.5 (AP)	Y
	TECHNETIUM TC 99M DEPREOTIDE	Diatide	13.6	FDA First Action: 6.0 (AE)	Y
				Sponsor Response: 1.8	
				FDA Second Action: 5.8 (AP)	Y
	FERRIC SODIUM GLUCONATE	R and D Labs	13.6	FDA First Action: 6.0 (AE)	Y
				Sponsor Response: 1.7	
				FDA Second Action: 6.0 (AP)	Y
	DENILEUKIN DIFTITOX (BLA)	Seragen, Inc.	13.9	FDA First Action: 6.0 (RL)	Y
				Sponsor Response: 1.9	
				FDA Second Action: 5.9 (AP)	Y

Table 2

FY 1998 Standard NDA and BLA Submissions Approved in FY 98 (✓) and FY 99

	Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
			Total Time	Resubmissions (if necessary)	
✓	IOVERSOL	Mallinckrodt Medcl	7.9		Y
	PAROXETINE HYDROCHLORIDE (CAPSULE)	SKB Pharms	9.5		Y
	ESTRADIOL	Novo Nordisk	9.7		Y
	OXYCODONE HYDROCHLORIDE	Roxane	9.9		Y
	VERAPAMIL HYDROCHLORIDE	Elan Pharm	10.9		Y
	ITRACONAZOLE	Janssen	11.1		Y
	FLUOXETINE HYDROCHLORIDE	Lilly	11.6		Y
	METRONIDAZOLE	Galderma	11.7		Y
	SYNTHETIC CONJUGATED ESTROGENS	Duramed Pharms	11.8		Y
	SEVELAMER HYDROCHLORIDE	Geltex	11.9		Y
	IBUPROFEN	Whitehall Robins	11.9		Y
	HUMAN INSULIN	Novo Nordisk	11.9		Y
	OXYBUTYNIN CHLORIDE	Alza	11.9		Y
	CERNEVIT-12 MULTIVITAMINS	Baxter Hlthcare	11.9		Y
	TROVAFLOXACIN MESYLATE / AZITHROMYCIN ***	Pfizer	12.0		Y
	ESTRADIOL /NORETHINDRONATE ACETATE	Novo Nordisk	12.0		Y
	AMOXICILLIN (TABLET)	SKB Pharms	12.0		Y
	AMOXICILLIN (POWDER)	SKB Pharms	12.0		Y
	CLOTRIMAZOLE	Schering Plough	12.0[1]		Y
	MICONAZOLE NITRATE	Advanced Care Prods	12.0		Y
	METHOXSALEN	Therakos	12.0		Y
	CALCITRIOL	Roche	12.0		Y
	MYCOPHENOLATE MOFETIL	Roche	12.0		Y
	RAPACURONIUM BROMIDE	Organon	13.8	FDA First Action: 9.9 (AE) Sponsor Response: 1.9 FDA Second Action: 2.0 (AP)	Y Y
	PAROXETINE HYDROCHLORIDE (TABLET)	SKB Pharms	13.9	FDA First Action: 9.7 (AE) Sponsor Response: 2.4 FDA Second Action: 1.9 (AP)	Y Y
	DOXERCALCIFEROL	Bone Care	15.0		Y **
	LEVOBUPIVACAINE	Darwin Discovery	15.3	FDA First Action: 10.0 (AE) Sponsor Response: 3.4 FDA Second Action: 1.9 (AP)	Y Y
	RABEPRAZOLE SODIUM	Eisai (US)	16.6	FDA First Action: 10.0 (AE) Sponsor Response: 1.2 FDA Second Action: 5.5 (AP)	Y Y

Table 2 (continued)

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
CIMETIDINE	SKB Pharms	18.3	FDA First Action: 11.6(AE)	Y
			Sponsor Response: 0.8	
			FDA Second Action: 5.9 (AP)	Y
RITONAVIR	Abbott Labs	19.1	FDA First Action: 12.0(NA)	Y
			Sponsor Response: 3.3	
			FDA Second Action: 3.9 (AP)	Y
ZALEPLON	Wyeth Ayerst Labs	19.2	FDA First Action: 12.0 (AE)	Y
			Sponsor Response: 1.8	
			FDA Second Action: 5.4 (AP)	Y

[1] This application was withdrawn on 29-Jan-96 because of insufficient data (new patients had to be enrolled and new data submitted). It was resubmitted on 25-Nov-97. This date was used to calculate all times. The original receipt date was 27-Apr-95.

*** This application was submitted on 19-Dec-1997, approved 18-Dec-1998, and then withdrawn on 22-Sep-99.

Table 3
FY 1997 Priority NDA and BLA Submissions Approved in FY 99

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
DALFOPRISTIN/QUINUPRISTIN	Rhone Poulenc Rorer	7.8[2]	FDA First Action: 6.0 (AE)	Y
			Sponsor Response: 16.7	
			FDA Second Action: 1.9 (AP)	Y
CAFFEINE CITRATE	Opr Develop LP	24.9	FDA First Action: 6.0 (AE)	Y
			Sponsor Response: 13.0	
			FDA Second Action: 6.0 (AP)	Y
ORLISTAT	Roche	28.8	FDA First Action: 9.0 (WD)	Y **
			Sponsor Response: 2.7	
			FDA Second Action: 5.8 (AE)	Y
			Sponsor Response: 8.3	
			FDA Third Action: 3.1 (AP)	Y

[2] The total approval time was adjusted because of a negative plant inspection. The time period until an acceptable inspection was received (05-Mar-98 to 26-Jul-99) was excluded from this time.

Table 4
FY 1997 Standard NDA and BLA Submissions Approved in FY 99

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
TELMISARTAN	Boehringer Ingelheim	13.5	FDA First Action: 12.0 (AE) Sponsor Response: 1.3 FDA Second Action: 0.2 (AP)	Y Y
DALFOPRISTIN/QUINUPRISTIN	Rhone Poulenc Rorer	13.8[3]	FDA First Action: 12.0 (AE) Sponsor Response: 10.7 FDA Second Action: 1.9 (AP)	Y Y
TOPIRAMATE	RW Johnson	14.8	FDA First Action: 11.6 (AE) Sponsor Response: 1.2 FDA Second Action: 2.0 (AP)	Y Y
LYME DISEASE VACCINE (Recombinant OspA) (PLA)	SmithKline Beecham Biologicals	15.2	FDA First Action: 10.5 (RL) Sponsor Response: 1.4 FDA Second Action: 3.2 (AP)	Y Y
GABAPENTIN	Parke Davis	15.3	FDA First Action: 12.0 (NA) Sponsor Response: 1.4 FDA Second Action: 1.9 (AP)	Y Y
CILOSTAZOL	Otsuka Pharm	15.9	FDA First Action: 12.0 (AE) Sponsor Response: 1.9 FDA Second Action: 2.0 (AP)	Y Y
13 C-UREA	Alimenterics	17.3	FDA First Action: 12.0 (NA) Sponsor Response: 3.6 FDA Second Action: 1.7 (AP)	Y Y
INTERFERON ALFA-N1 (LYMPHOBLASTOID) (PLA)	Wellcome Foundation Limited, Wellcome Research Laboratories	17.8	FDA First Action: 11.9 (RL) Sponsor Response: 2.0 FDA Second Action: 2.0 (RL) Sponsor Response: 0.4 FDA Third Action: 1.5 (AP)	Y Y Y
ONDANSETRON	Glaxo Wellcome	18.9	FDA First Action: 12.0 (AE) Sponsor Response: 0.9 FDA Second Action: 6.0 (AP)	Y Y
LEVALBUTEROL HYDROCHLORIDE	Sepracor	20.8	FDA First Action: 12.0 (AE) Sponsor Response: 2.8 FDA Second Action: 6.0 (AP)	Y Y

Table 4 (continued)

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
PROGESTERONE	Schering Plough	21.2	FDA First Action: 12.0 (AE) Sponsor Response: 5.6 FDA Second Action: 3.6 (AP)	Y Y
FAMOTIDINE	Merck Res	22.2	FDA First Action: 12.0 (AE) Sponsor Response: 2.7 FDA Second Action: 6.0 (AE) Sponsor Response: 0.4 FDA Third Action: 1.1 (AP)	Y Y Y
ANTI-THYMOCYTE GLOBULIN (RABBIT) (PLA)	Pasteur Merieux Serums et Vaccins, S.A.	23.4	FDA First Action: 12.0 (RL) Sponsor Response: 1.3 FDA Second Action: 4.7 (RL) Sponsor Response: 0.6 FDA Third Action: 4.8 (AP)	Y Y Y
FENTANYL CITRATE	Anesta	23.7	FDA First Action: 12.0 (NA) *Sponsor Response: 5.7* FDA Second Action: 6.0 (AP)	Y Y
MODAFINIL	Cephalon	23.8	FDA First Action: 12.0 (AE) Sponsor Response: 0.0 FDA Second Action: 5.8 (AP)	Y Y

[3] The total approval time was adjusted because of a negative plant inspection. The time period until an acceptable inspection was received (04-Sep-98 to 26-Jul-99) was excluded from this time.

Table 5
FY 1996 Priority NDA and BLA Submissions Approved in FY 99

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
COAGULATION FACTOR VIIa (Recombinant) (BLA)	Novo Nordisk A/S	34.5	FDA First Action: 11.6 (NA) Sponsor Response: 5.3 FDA Second Action: 5.4 (RL) Sponsor Response: 1.0 FDA Third Action: 6.0 (RL) Sponsor Response: 2.8 FDA Fourth Action: 2.4 (AP)	Y Y Y Y

Table 6
FY 1996 Standard NDA and BLA Submissions Approved in FY 99

Generic Name	Sponsor	Approval Time (Months)		Review Goal Met
		Total Time	Resubmissions (if necessary)	
SIMETHICONE- CELLULOSE	Bracco DXS	25.0	FDA First Action: 12.0 (NA) Sponsor Response: 7.0 FDA Second Action: 6.0 (AP)	Y Y
ANTIHEMOPHILIC FACTOR / VON WILLEBRAND FACTOR COMPLEX (HUMAN) (BLA)	*Centeon Pharma GmbH*	30.5	*FDA First Action: 15.0 (NA)* Sponsor Response: 4.2 FDA Second Action: 5.8 (RL) Sponsor Response: 5.1 FDA Third Action: 0.5 (AP)	Y Y Y
LIDOCAINE	Teikoku Pharma USA	33.2	FDA First Action: 10.2 (NA) Sponsor Response: 13.5 FDA Second Action: 6.0 (AE) Sponsor Response: 1.6 FDA Third Action: 1.9 (AP)	Y Y Y
POLYETHYLENE GLYCOL 3350	Braintree Labs	35.7	FDA First Action: 11.9 (NA) Sponsor Response: 15.3 FDA Second Action: 6.0 (AE) Sponsor Response: 0.5 FDA Third Action: 2.0 (AP)	Y Y Y

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