M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: March 26, 1999

To: Dockets Management Branch (HFA-305)

From: Ted Sherwood
Management Analyst
Office of Generic Drugs

Subject: Written Materials Regarding Human Generic Drugs to Docket 90S-0308

This memorandum forwards written materials to the Dockets Management Branch for inclusion in Docket 90S-0308. This material is "Center for Drug Evaluation and Research - Office of Generic Drugs Quantitative Reports for February 1999 - ANDAs" (10 pages).

Ted Sherwood

Attachment

174

90S-0308

M 634
174

Center for Drug Evaluation and Research - Office of Generic Drugs
Quantitative Report

ORIGINAL APPLICATIONS

	Mar-98	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
TOTAL ORIGINALS	20	24	27	27	26	34	26	24	39	47	27	25	346	29	33	27
AMENDMENTS	125	101	92	103	100	112	116	129	109	130	107	123	1347	112	120	107
- MAJOR	66	58	50	51	59	70	62	61	44	62	40	76	699	58	59	49
- MINOR	31	26	18	28	21	20	24	24	29	32	27	18	298	25	26	34
- FACSIMILE**	28	17	24	24	20	22	30	44	36	36	40	29	350	29	35	24
--ACTIONS--																
APPROVALS	15	22	11	19	22	19	26	13	17	28	10	14	216	18	17	22
TENTATIVE APPROVALS+	0	1	2	2	2	3	2	10	9	6	6	5	48	4	6	3
NOT APPROVABLE	45	39	34	40	40	34	32	34	50	29	16	27	420	35	24	40
FACSIMILE REQUEST**	22	9	15	22	15	24	22	26	15	20	9	20	219	18	16	16
REFUSE TO FILE	5	1	6	4	4	2	9	5	5	10	6	11	68	6	9	7
WITHDRAWALS	1	49	7	4	70	7	24	97	4	37	16	2	318	27	18	39
- OF APPROVED	1	30	5	4	61	5	17	93	2	16	14	0	248	21	10	32
- OF UNAPPROVED	0	19	2	0	9	2	7	4	2	21	2	2	70	6	8	7
--REVIEW STATUS--																
AWAITING OGD ACTION (TOTAL)***	413	412	422	418	399	421	417	405	407	422	438	442		418	434	384
AWAITING OGD ACTION (> 180 DAYS)	75	79	87	91	87	87	97	99	88	88	79	105		89	91	72
AWAITING OGD ACTION (<=180 DAYS)	338	333	335	327	312	334	320	306	319	334	359	337		330	343	312

* - Please see page titled "Old Counting System" for numbers represented by the old counting system as reported in prior months.

** - Facsimile policy went into effect in January of 1997

***- In September, 1991, the Office of Generic Drugs started implementation of its Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. Review status figures reported since this date exclude suspended applications. As of February 28, 1999, 0 original applications and 18 supplements were suspended. Upon completion of validity assessments, suspended applications may be returned to active pending status.

+ - Note: Tentative approvals are counted as approvals subsequently when approved. For example 21 of the 216 approvals for the year ending February 28, 1999, were previously reported as tentatively approved applications.

Center for Drug Evaluation and Research - Office of Generic Drugs
Quantitative Report

POST APPROVAL SUBMISSIONS TO APPLICATIONS (CHEMISTRY)

	Mar-98	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
ORIGINAL SUPPLEMENTS	195	350	128	393	200	314	366	197	211	389	188	150	3081	257	242	200
AMENDMENTS TO SUPPLEMENTS	228	334	139	394	161	336	134	205	286	156	125	158	2656	221	146	166
--SUPPLEMENTAL ACTIONS-																
APPROVALS**	174	146	155	134	112	138	152	187	174	446	39	310	2167	181	265	168
APPROVABLE	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NOT APPROVABLE	104	64	55	96	58	72	102	50	68	77	21	77	844	70	58	62
WITHDRAWALS	16	16	16	25	20	2	8	11	8	84	1	11	218	18	32	22
--REVIEW STATUS--																
SUPPLEMENTS AWAITING* OGD ACTION (TOTAL)	1081	1307	1268	1473	1553	1726	1862	1925	1905	1749	1866	1737		1621	1784	1198
SUPPLEMENTS AWAITING OGD ACTION (>180 DAYS)	130	92	83	89	101	152	141	251	213	234	243	237		164	238	98
SUPPLEMENTS AWAITING OGD ACTION (<=180 DAYS)	951	1215	1185	1384	1452	1574	1721	1674	1692	1515	1623	1500		1457	1546	1099

* - In September, 1991, the Office of Generic Drugs started implementation of its Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. Review status figures reported since this date exclude suspended applications. As of February 28, 1999, 0 original applications and 18 supplements were suspended. Upon completion of validity assessments, suspended applications may be returned to active pending status.

** The February 1998 chemistry supplemental approvals include 216 global submissions.

Center for Drug Evaluation and Research - Office of Generic Drugs
Quantitative Report

POST APPROVAL SUBMISSIONS TO APPLICATIONS (LABELING)

	Mar-98	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
ORIGINAL SUPPLEMENTS	28	53	79	73	69	34	34	94	46	59	41	33	643	54	44	51
AMENDMENTS TO SUPPLEMENTS	32	48	79	72	62	69	45	67	40	78	55	49	696	58	61	51
--SUPPLEMENTAL ACTIONS-																
APPROVALS	77	64	39	62	28	119	61	60	46	39	39	31	665	55	36	43
APPROVABLE	9	7	17	9	10	7	7	4	6	13	4	17	110	9	11	9
NOT APPROVABLE	13	12	30	8	18	18	15	8	7	17	5	5	156	13	9	14
WITHDRAWALS	3	3	5	2	7	1	4	1	3	0	0	4	33	3	1	3
--REVIEW STATUS--																
SUPPLEMENTS AWAITING OGD ACTION (TOTAL)	361	355	354	389	401	317	287	303	314	318	338	339		340	332	382
SUPPLEMENTS AWAITING OGD ACTION (>180 DAYS)	161	151	132	152	137	110	112	109	120	125	137	116		130	126	154
SUPPLEMENTS AWAITING OGD ACTION (<=180 DAYS)	200	204	222	237	264	207	175	194	194	193	201	223		210	206	228

* - In September, 1991, the Office of Generic Drugs started implementation of its Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. Review status figures reported since this date exclude suspended applications. As of February 28, 1999, 0 original applications and 18 supplements were suspended. Upon completion of validity assessments, suspended applications may be returned to active pending status.

Center for Drug Evaluation and Research - Office of Generic Drugs
Quantitative Report

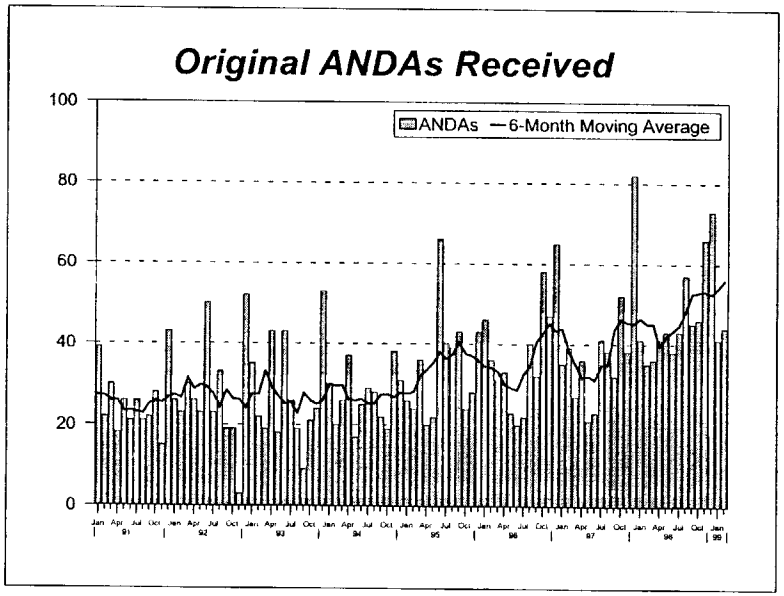
ORIGINAL APPLICATIONS - OLD COUNTING SYSTEM

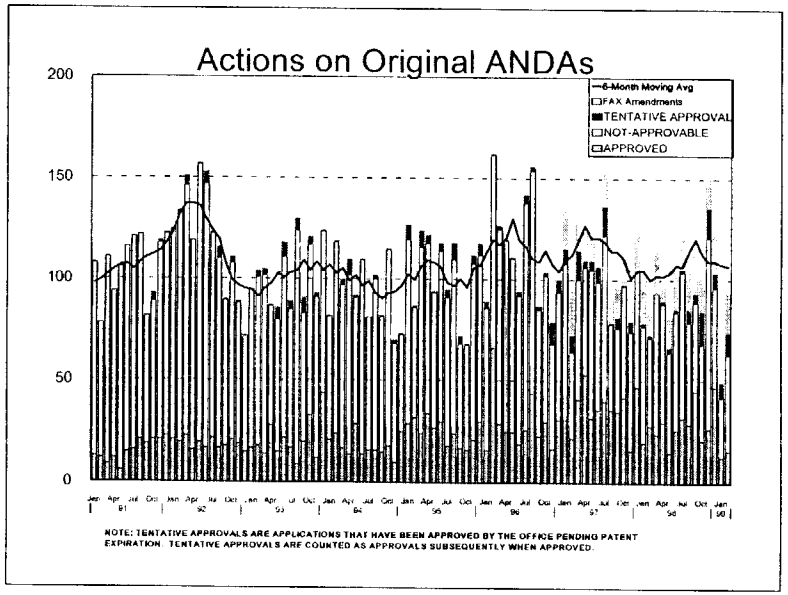
	Mar-98	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
TOTAL ORIGINALS	36	41	43	38	43	57	45	46	66	73	41	44	573	48	53	39
AMENDMENTS	125	101	92	103	100	112	116	129	109	130	107	123	1347	112	120	107
- MAJOR	66	58	50	51	59	70	62	61	44	62	40	76	699	58	59	49
- MINOR	31	26	18	28	21	20	24	24	29	32	27	18	298	25	26	34
- FACSIMILE	28	17	24	24	20	22	30	44	36	36	40	29	350	29	35	24
--ACTIONS--																
APPROVALS	24	30	15	26	32	29	45	21	27	47	13	16	325	27	25	36
TENTATIVE APPROVALS+	0	2	3	2	2	7	5	17	15	8	8	11	80	7	9	5
NOT APPROVABLE	70	58	49	58	72	50	44	47	94	49	29	47	667	56	42	57
FACSIMILE REQUEST*	22	9	15	22	15	24	22	26	15	20	9	20	219	18	16	16
REFUSE TO FILE	11	1	12	6	6	4	14	10	8	13	6	12	103	9	10	9
WITHDRAWALS	1	56	7	5	73	7	27	97	4	41	18	5	341	28	21	41
- OF APPROVED	1	30	5	5	62	5	20	93	2	17	14	0	254	21	10	33
- OF UNAPPROVED	0	26	2	0	11	2	7	4	2	24	4	5	87	7	11	9
--REVIEW STATUS--																
AWAITING OGD ACTION(TOTAL)**	613	615	641	642	608	654	655	647	647	677	709	719		652	702	570
AWAITING OGD ACTION (>180 DAYS)	108	117	127	143	134	130	142	147	122	138	118	153		132	136	113
AWAITING OGD ACTION (< =180DAYS)	505	498	514	499	474	524	513	500	525	539	591	566		521	565	457

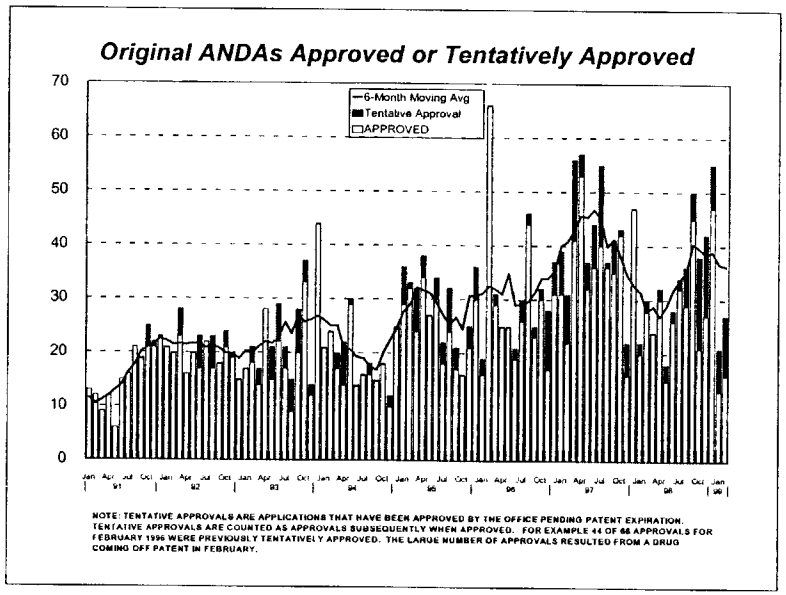
* - Facsimile policy went into effect in January of 1997

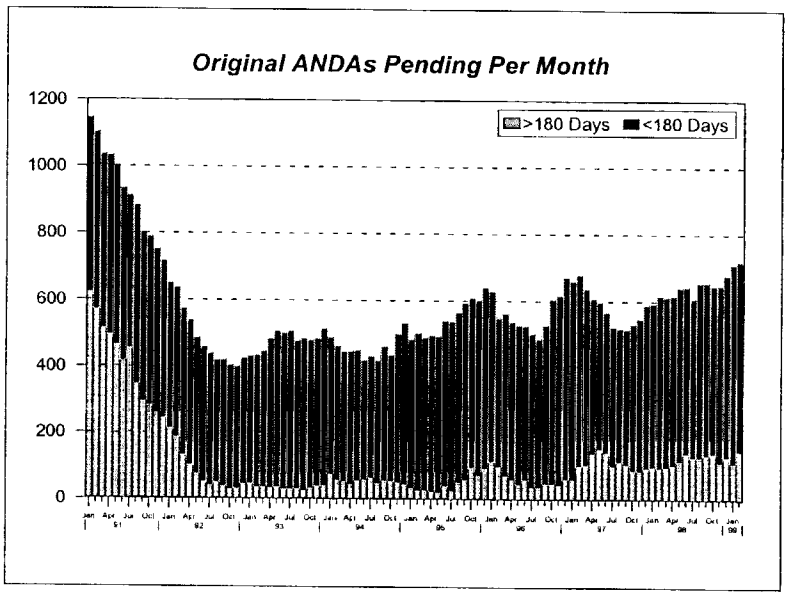
** - In September, 1991, the Office of Generic Drugs started implementation of its Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. Review status figures reported since this date exclude suspended applications. As of February 28, 1999, 0 original applications and 18 supplements were suspended. Upon completion of validity assessments, suspended applications may be returned to active pending status.

\+ - Note: Tentative approvals are counted as approvals subsequently when approved. For example 21 of the 325 approvals for the year ending February 28, 1999, were previously reported as tentatively approved applications.

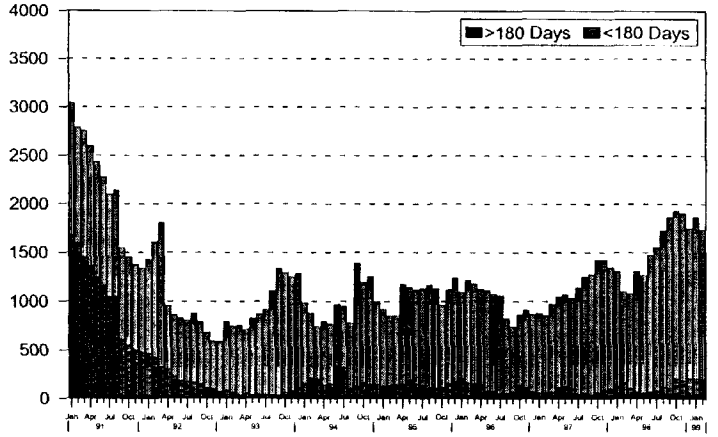

Original ANDAs Received
ANDAs
6-Month Moving Average
100
80
60
40
20
0


Actions on Original ANDAs
6-Month Moving Avg
FAX Amendments
TENTATIVE APPROVAL
NOT-APPROVABLE
APPROVED
200
150
100
50
0
NOTE: TENTATIVE APPROVALS ARE APPLICATIONS THAT HAVE BEEN APPROVED BY THE OFFICE PENDING PATENT EXPIRATION. TENTATIVE APPROVALS ARE COUNTED AS APPROVALS SUBSEQUENTLY WHEN APPROVED.


Original ANDAs Approved or Tentatively Approved
6-Month Moving Avg
Tentative Approval
APPROVED
70
60
50
40
30
20
10
0
NOTE: TENTATIVE APPROVALS ARE APPLICATIONS THAT HAVE BEEN APPROVED BY THE OFFICE PENDING PATENT EXPIRATION. TENTATIVE APPROVALS ARE COUNTED AS APPROVALS SUBSEQUENTLY WHEN APPROVED. FOR EXAMPLE 44 OF 66 APPROVALS FOR FEBRUARY 1996 WERE PREVIOUSLY TENTATIVELY APPROVED. THE LARGE NUMBER OF APPROVALS RESULTED FROM A DRUG COMING OFF PATENT IN FEBRUARY.

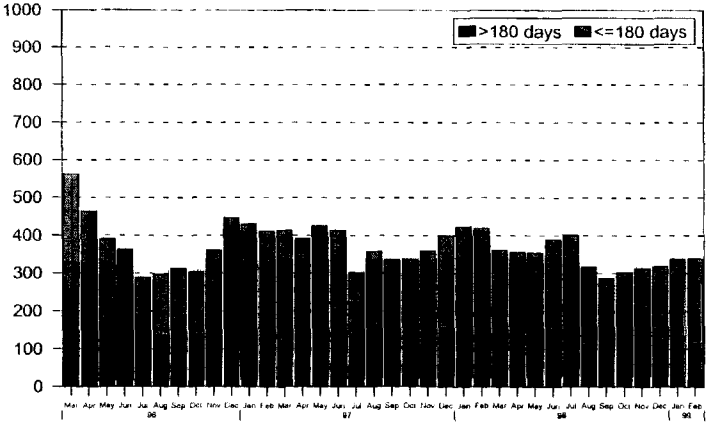

Original ANDAs Pending Per Month
>180 Days
<180 Days
1200
1000
800
600
400
200
0

Chemistry, Manufacturing & Controls Supplements Awaiting OGD Action

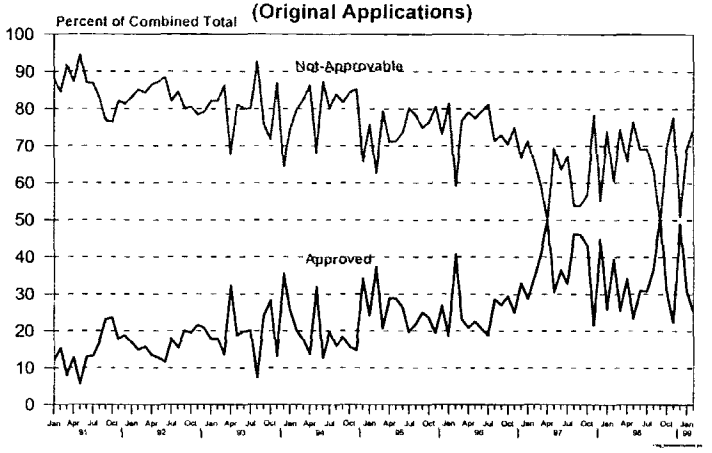


Please note that abrupt changes in the level of pending supplements (e.g. the increase in September 1994) are the result of global submissions to all applications held by a single firm. Changes other than these will be explained separately.

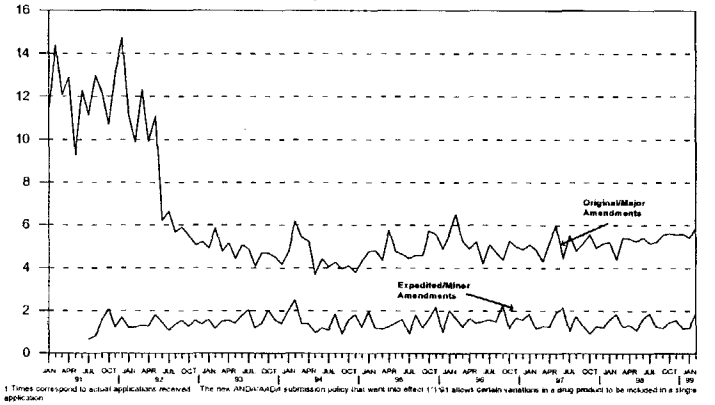
Labeling Supplements Awaiting OGD Action



Percent Approved and Not-Approvable Per Month (Original Applications)



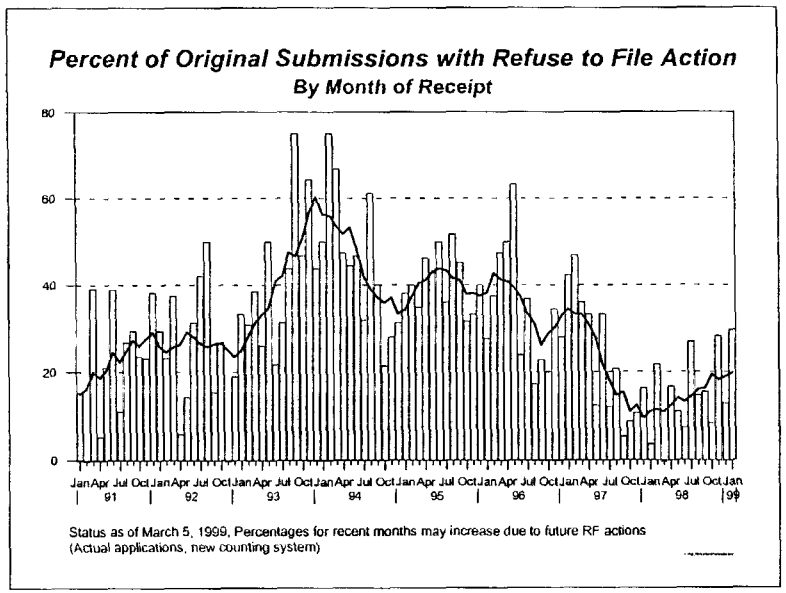
Median ANDA CMC Supplement Review Time (Months)

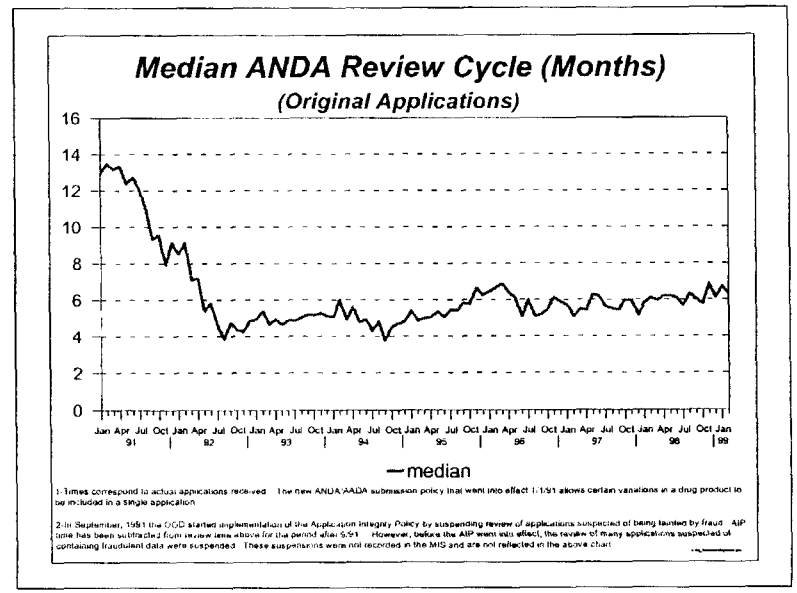


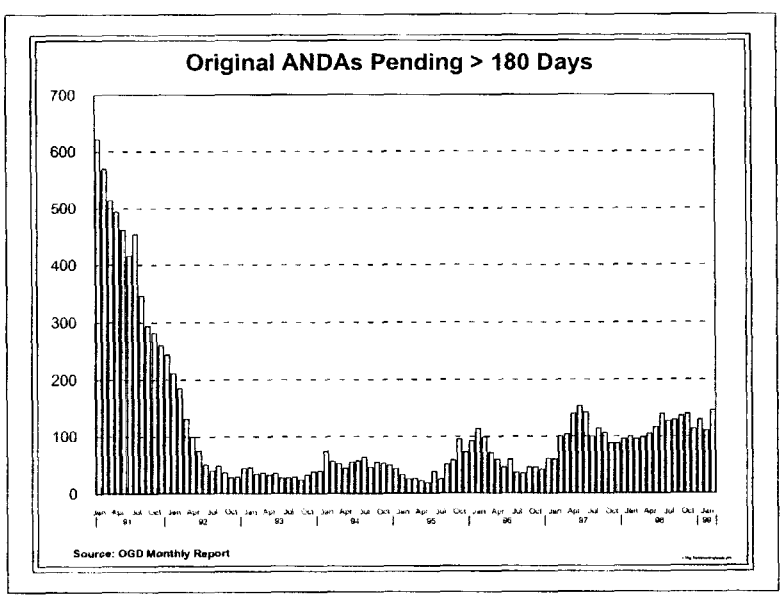
1 Times correspond to actual applications received. The new ANDA/AADA submission policy that went into effect 11/91 allows certain variations in a drug product to be included in a single application.

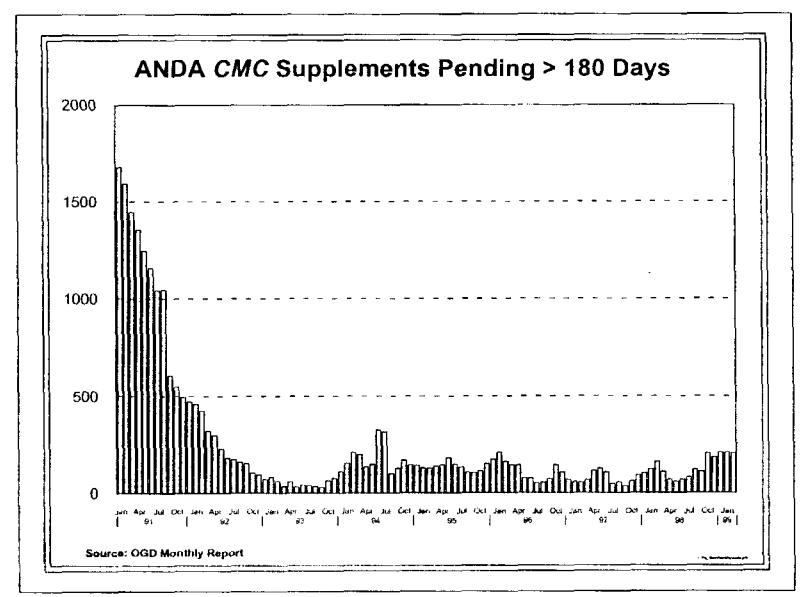
2 In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. AIP time has been subtracted from review time above for the period after 9/91. However, before the AIP went into effect, the review of many applications suspected of containing fraudulent data were suspended. These suspensions were not recorded in the MIS and are not reflected in the above chart.

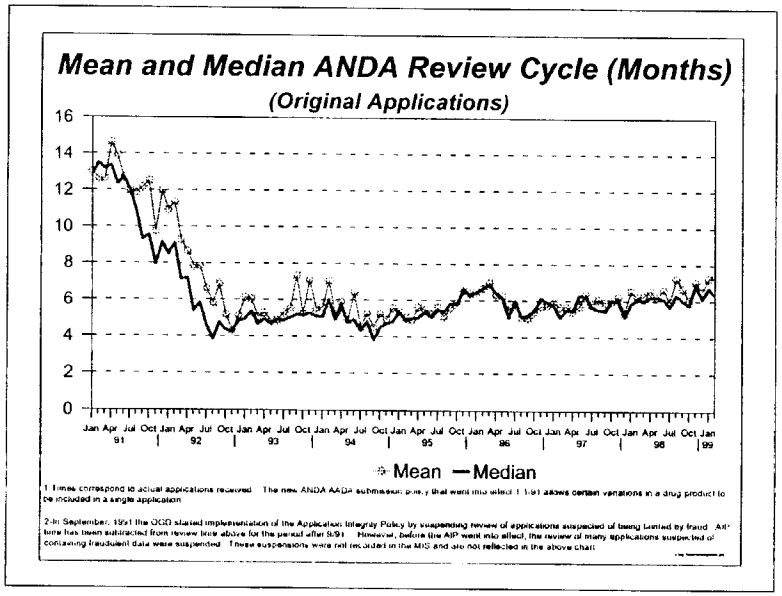
Note: Global Supplements Collapsed


Percent of Original Submissions with Refuse to File Action
By Month of Receipt
80
60
40
20
0
Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan
91 92 93 94 95 96 97 98 99
Status as of March 5, 1999, Percentages for recent months may increase due to future RF actions
(Actual applications, new counting system)


Median ANDA Review Cycle (Months)
(Original Applications)
16
14
12
10
8
6
4
2
0
Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan
91 92 93 94 95 96 97 98 99
median
1-Times correspond to actual applications received. The new ANDA/AADA submission policy that went into effect 1/1/91 allows certain variations in a drug product to be included in a single application.
2-In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. AIP time has been subtracted from review time above for the period after 9/91. However, before the AIP went into effect, the review of many applications suspected of containing fraudulent data were suspended. These suspensions were not recorded in the MIS and are not reflected in the above chart.


Original ANDAs Pending > 180 Days
700
600
500
400
300
200
100
0
Source: OGD Monthly Report


ANDA CMC Supplements Pending > 180 Days
2000
1500
1000
500
0
Source: OGD Monthly Report


Mean and Median ANDA Review Cycle (Months)
(Original Applications)
16
14
12
10
8
6
4
2
0
Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan Apr Jul Oct Jan
91 92 93 94 95 96 97 98 99
Mean
Median
1 Times correspond to actual applications received. The new ANDA AADA submission policy that went into effect 11/91 allows certain variations in a drug product to be included in a single application
2-In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. Additions has been subtracted from review time above for the period after 9/91. However, before the AIP was into effect, the review of many applications suspected of containing fraudulent data were suspended. These suspensions were not recorded in the MIS and are not reflected in the above chart.

Office of Generic Drugs ANDAs Approvals

1.	75-391	CLOBETASOL PROPIONATE TOPICAL SOLUTION, USP 0.05%	ALTANA, INC.	02/08/99
2.	75-063	ALBUTEROL SULFATE INHALATION SOLUTION 0.083% (BASE)	HI-TECH PHARMACAL CO., INC.	02/09/99
3.	75-188	AMIODARONE HYDROCHLORIDE TABLETS 200 MG	ALPHAPHARM PTY. LIMITED	02/24/99
4.	75-340	HYDROXYUREA CAPSULES, USP 500 MG	PAR PHARMACEUTICAL, INC.	02/24/99
5.	75-065	ACYCLOVIR SODIUM INJECTION 50 MG (BASE)/ML; 500 MG AND 1 G VIALS.	MERIDIAN MEDICAL TECHNOLOGIES, INC.	02/25/99
6.	40-266	* METHOTREXATE FOR INJECTION, USP (PRESERVATIVE-FREE) 1 G/VIAL	BIGMAR, INC.	02/26/99
7.	74-986	DICLOFENAC SODIUM DELAYED-RELEASE TABLETS, USP 50 MG, 75 MG	MARTEC SCIENTIFIC, INC.	02/26/99
8.	40-265	* METHOTREXATE INJECTION, USP (PRESERVATIVE-FREE) 25 MG/ML	BIGMAR, INC.	02/26/99
9.	64-216	* COLISTIMETHATE FOR INJECTION, USP 150 MG (BASE)/VIAL	PHARMA-TEK, INC.	02/26/99
10.	40-263	METHOTREXATE INJECTION, USP (PRESERVED) 25 MG/ML	BIGMAR, INC.	02/26/99
11.	75-153	* PSEUDOEPHEDRINE HYDROCHLORIDE EXTENDED-RELEASE TABLETS 120 MG	L. PERRIGO COMPANY	02/26/99
12.	40-258	LEUCOVORIN CALCIUM FOR INJECTION (PRESERVATIVE-FREE) 200 MG (BASE)/VIAL	BIGMAR, INC.	02/26/99
13.	40-286	* LEUCOVORIN CALCIUM FOR INJECTION, (PRESERVATIVE-FREE) 500 MG (BASE)/VIAL	BIGMAR, INC.	02/26/99
14.	40-230	DICYCLOMINE HYDROCHLORIDE TABLETS, USP 20 MG	LANNETT COMPANY, INC.	02/26/99

1.	75-355		LABETALOL HYDROCHLORIDE INJECTION, USP 5 MG/ML	APOTHECON, INC.	02/23/99
2.	75-091	*	CARBIDOPA AND LEVODOPA EXTENDED-RELEASE TABLETS 50 MG/200 MG	MYLAN PHARMACEUTICALS, INC.	02/26/99
3.	75-207	*	FLUOXETINE CAPSULES, USP 10 MG, 20 MG	MYLAN PHARMACEUTICALS, INC.	02/26/99
4.	75-301	*	DOXAZOSIN MESYLATE TABLETS 1 MG (BASE), 2 MG (BASE), 4 MG (BASE), 8 MG (BASE)	GENEVA PHARMACEUTICALS, INC.	02/26/99
5.	75-138	*	VERAPAMIL HYDROCHLORIDE EXTENDED-RELEASE CAPSULES 120 MG, 180 MG, 240 MG	MYLAN PHARMACEUTICALS, INC.	02/26/99