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: April 8, 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 March 1999 - ANDAs" (10 pages).

Ted Sherwood

Attachment

90S-0308

M 635
185

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

TABLE I

ORIGINAL APPLICATIONS

	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	Mar-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
TOTAL ORIGINALS	24	27	27	26	34	26	24	39	47	27	25	22	348	29	25	27
AMENDMENTS	101	92	103	100	112	116	129	109	130	107	123	163	1385	115	131	108
- MAJOR	58	50	51	59	70	62	61	44	62	40	76	74	707	59	63	51
- MINOR	26	18	28	21	20	24	24	29	32	27	18	45	312	26	30	34
- FACSIMILE**	17	24	24	20	22	30	44	36	36	40	29	44	366	31	38	24
--ACTIONS--																
APPROVALS	22	11	19	22	19	26	13	17	28	10	14	15	216	18	13	21
TENTATIVE APPROVALS+	1	2	2	2	3	2	10	9	6	6	5	5	53	4	5	2
NOT APPROVABLE	39	34	40	40	34	32	34	50	29	16	27	55	430	36	33	40
FACSIMILE REQUEST**	9	15	22	15	24	22	26	15	20	9	20	20	217	18	16	17
REFUSE TO FILE	1	6	4	4	2	9	5	5	10	6	11	3	66	6	7	7
WITHDRAWALS	49	7	4	70	7	24	97	4	37	16	2	10	327	27	9	35
- OF APPROVED	30	5	4	61	5	17	93	2	16	14	0	2	249	21	5	29
- OF UNAPPROVED	19	2	0	9	2	7	4	2	21	2	2	8	78	7	4	6
--REVIEW STATUS--																
AWAITING OGD ACTION (TOTAL)***	412	422	418	399	421	417	405	407	422	438	442	439		420	440	383
AWAITING OGD ACTION (> 180 DAYS)	79	87	91	87	87	97	99	88	88	79	105	98		90	94	72
AWAITING OGD ACTION (<=180 DAYS)	333	335	327	312	334	320	306	319	334	359	337	341		330	346	310

* - 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 March 31, 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 March 31, 1999, were previously reported as tentatively approved applications.

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

TABLE II

POST APPROVAL SUBMISSIONS TO APPLICATIONS (CHEMISTRY)

	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	Mar-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
ORIGINAL SUPPLEMENTS	350	128	393	200	314	366	197	211	389	188	150	148	3034	253	162	2
AMENDMENTS TO SUPPLEMENTS	334	139	394	161	336	134	205	286	156	125	158	404 ▲	2832	236	229	1
--SUPPLEMENTAL ACTIONS-																
APPROVALS	146	155	134	112	138	152	187	174	446	39	310	283 ●	2276	190	211	1
APPROVABLE	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
NOT APPROVABLE	64	55	96	58	72	102	50	68	77	21	77	328 ■	1068	89	142	
WITHDRAWALS	16	16	25	20	2	8	11	8	84	1	11	23	225	19	12	
--REVIEW STATUS--																
SUPPLEMENTS AWAITING* OGD ACTION (TOTAL)	1307	1268	1473	1553	1726	1862	1925	1905	1749	1866	1737	1362		1644	1655	12
SUPPLEMENTS AWAITING OGD ACTION (>180 DAYS)	92	83	89	101	152	141	251	213	234	243	237	128		164	203	1
SUPPLEMENTS AWAITING OGD ACTION (<=180 DAYS)	1215	1185	1384	1452	1574	1721	1674	1692	1515	1623	1500	1234		1481	1452	11

* - 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 statu figures reported since this date exclude suspended applications. As of March 31, 1999, 0 original applications and 18 supplements were suspended. Upon completion of validity assessments, suspended applications may be returned to active pending status.

▲ Includes 203 amendments to supplements submitted by one applicant.

● Includes approval of "global" supplements submitted by single applicants.

■ Includes a total of 290 not approvable actions taken on "global" supplements submitted by 2 individual applicants.

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

TABLE III

POST APPROVAL SUBMISSIONS TO APPLICATIONS (LABELING)

	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	Mar-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
ORIGINAL SUPPLEMENTS	53	79	73	69	34	34	94	46	59	41	33	61	676	56	45	49
AMENDMENTS TO SUPPLEMENTS	48	79	72	62	69	45	67	40	78	55	49	55	719	60	53	50
--SUPPLEMENTAL ACTIONS-																
APPROVALS	64	39	62	28	119	61	60	46	39	39	31	40	628	52	37	47
APPROVABLE	7	17	9	10	7	7	4	6	13	4	17	3	104	9	8	9
NOT APPROVABLE	12	30	8	18	18	15	8	7	17	5	5	23	166	14	11	14
WITHDRAWALS	3	5	2	7	1	4	1	3	0	0	4	25	55	5	10	3
--REVIEW STATUS--																
SUPPLEMENTS AWAITING OGD ACTION (TOTAL)	355	354	389	401	317	287	303	314	318	338	339	349		339	342	377
SUPPLEMENTS AWAITING OGD ACTION (>180 DAYS)	151	132	152	137	110	112	109	120	125	137	116	109		126	121	157
SUPPLEMENTS AWAITING OGD ACTION (<=180 DAYS)	204	222	237	264	207	175	194	194	193	201	223	240		213	221	220

* - 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 March 31, 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

TABLE IV

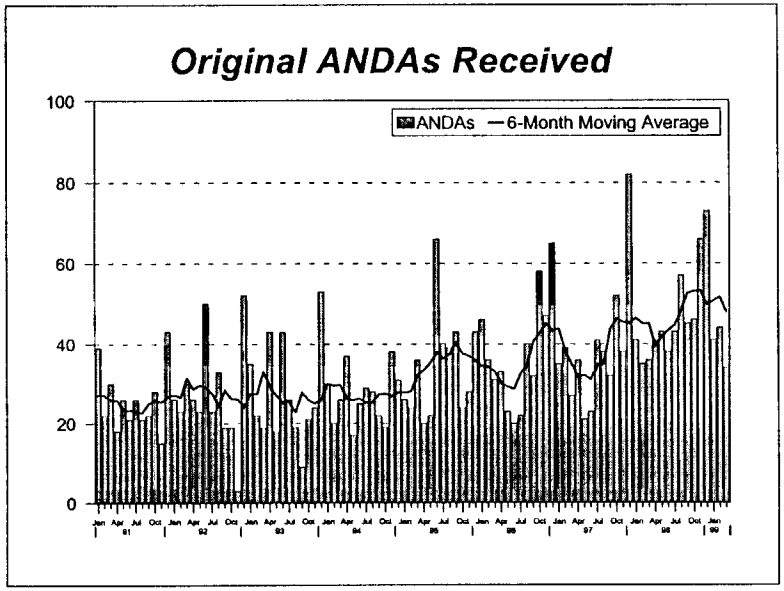
ORIGINAL APPLICATIONS - OLD COUNTING SYSTEM

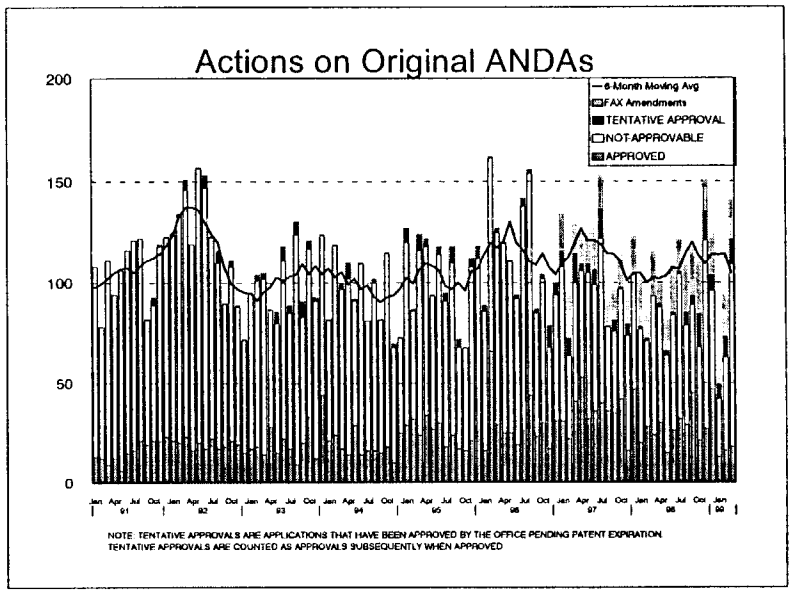
	Apr-98	May-98	Jun-98	Jul-98	Aug-98	Sep-98	Oct-98	Nov-98	Dec-98	Jan-99	Feb-99	Mar-99	TOTAL	AVG LAST 12 MOS	AVG LAST 3 MOS	AVG PRIOR YEAR
--RECEIPTS--																
TOTAL ORIGINALS	41	43	38	43	57	45	46	66	73	41	44	34	571	48	40	40
AMENDMENTS	101	92	103	100	112	116	129	109	130	107	123	163	1385	115	131	108
- MAJOR	58	50	51	59	70	62	61	44	62	40	76	74	707	59	63	51
- MINOR	26	18	28	21	20	24	24	29	32	27	18	45	312	26	30	34
- FACSIMILE	17	24	24	20	22	30	44	36	36	40	29	44	366	31	38	24
--ACTIONS--																
APPROVALS	30	15	26	32	29	45	21	27	47	13	16	18	319	27	16	34
TENTATIVE APPROVALS+	2	3	2	2	7	5	17	15	8	8	11	13	93	8	11	4
NOT APPROVABLE	58	49	58	72	50	44	47	94	49	29	47	91	688	57	56	58
FACSIMILE REQUEST*	9	15	22	15	24	22	26	15	20	9	20	20	217	18	16	17
REFUSE TO FILE	1	12	6	6	4	14	10	8	13	6	12	4	96	8	7	9
WITHDRAWALS	56	7	5	73	7	27	97	4	41	18	5	11	351	29	11	37
- OF APPROVED	30	5	5	62	5	20	93	2	17	14	0	2	255	21	5	29
- OF UNAPPROVED	26	2	0	11	2	7	4	2	24	4	5	9	96	8	6	8
--REVIEW STATUS--																
AWAITING OGD ACTION(TOTAL)**	615	641	642	608	654	655	647	647	677	709	719	714		661	714	568
AWAITING OGD ACTION (>180 DAYS)	117	127	143	134	130	142	147	122	138	118	153	154		135	142	113
AWAITING OGD ACTION (< =180DAYS)	498	514	499	474	524	513	500	525	539	591	566	560		525	572	455

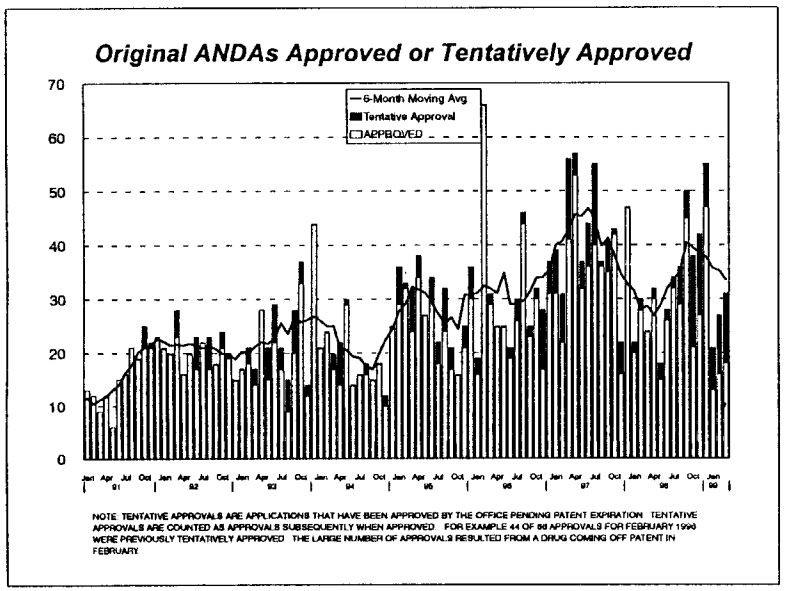
* - Facsimile policy went into effect in January of 1997

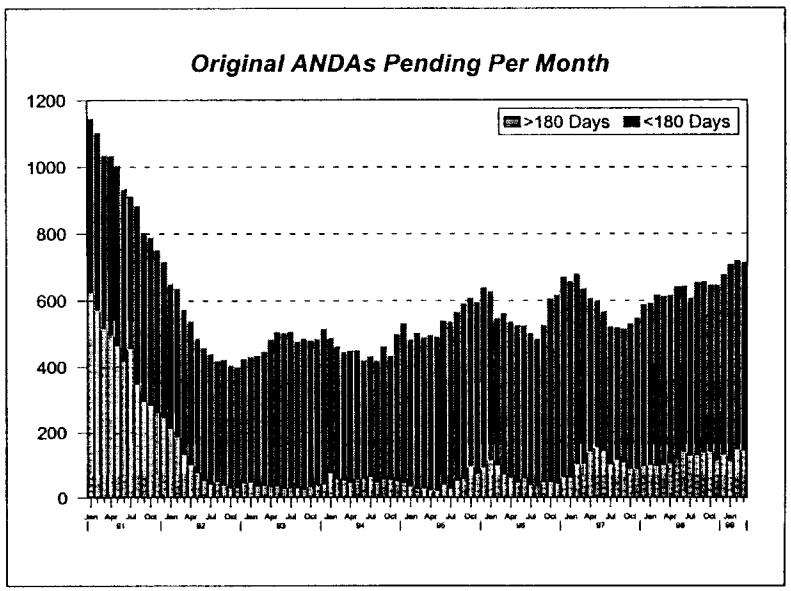
** - In September, 1991, the Office of Generic Drugs started implementation of its Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. Review status figures reported since this date exclude suspended applications. As of March 31, 1999, 0 original applications 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 319 approvals for the year ending March 31, 1999, were previously reported as tentatively approved applications.

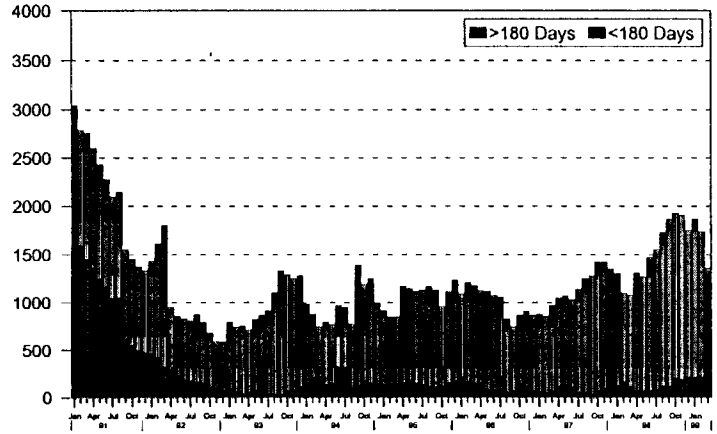

Original ANDAs Received
ANDAs
6-Month Moving Average
100
80
60
40
20
0


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 98 APPROVALS FOR FEBRUARY 1998 WERE PREVIOUSLY TENTATIVELY APPROVED. THE LARGE NUMBER OF APPROVALS RESULTED FROM A DRUG COMING OFF PATENT IN FEBRUARY.

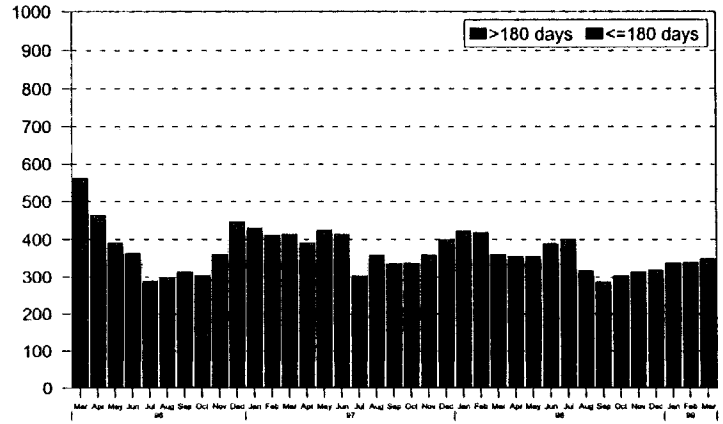

Original ANDAs Pending Per Month
>180 Days
<180 Days
1200
1000
800
600
400
200
0

Chemistry, Manufacturing & Controls Supplements Awaiting OGD Action



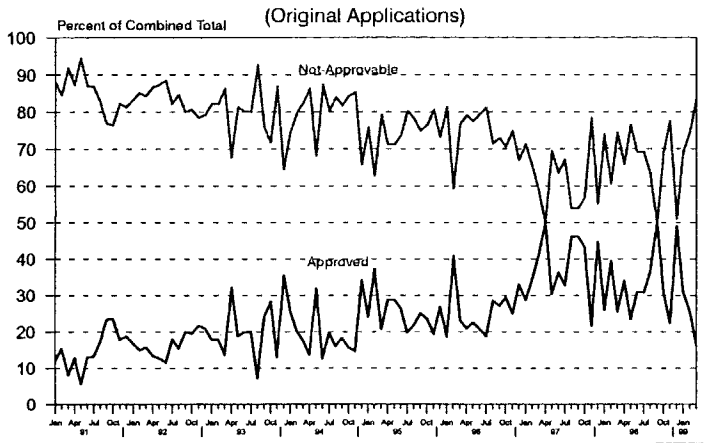
Please note that abrupt changes in the level of pending supplements (e.g. the increase in September 1994) are the result of global submissions to all applications held by a single firm. Changes other than these will be explained separately

Labeling Supplements Awaiting OGD Action



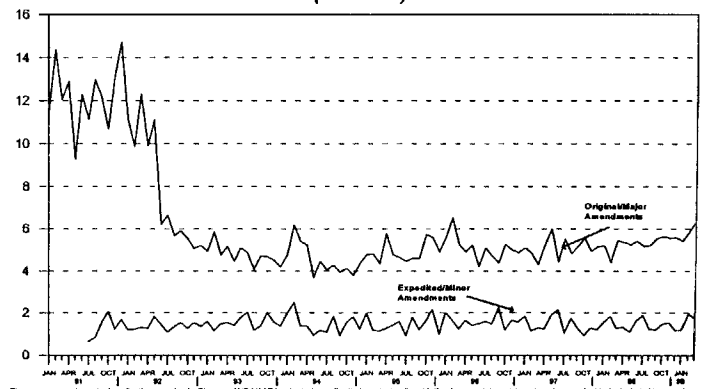
Percent Approved and Not-Approvable Per Month

(Original Applications)



Median ANDA CMC Supplement Review Time

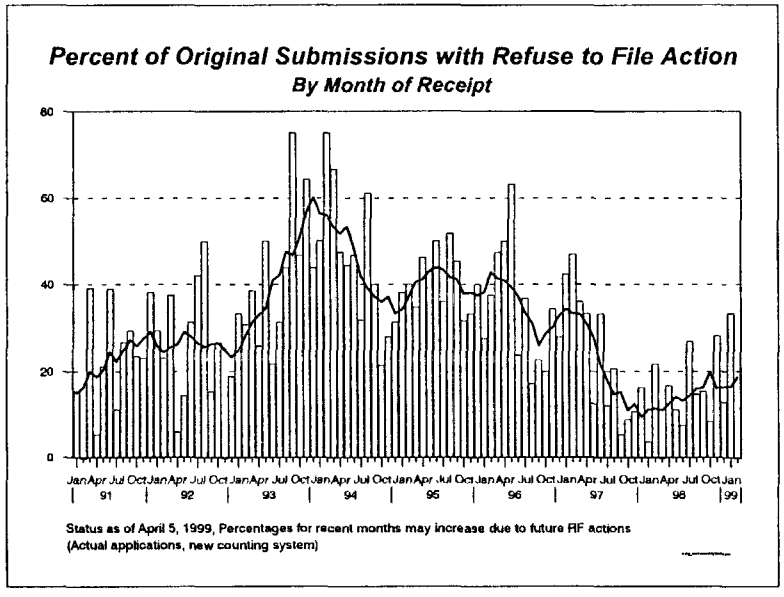
(Months)

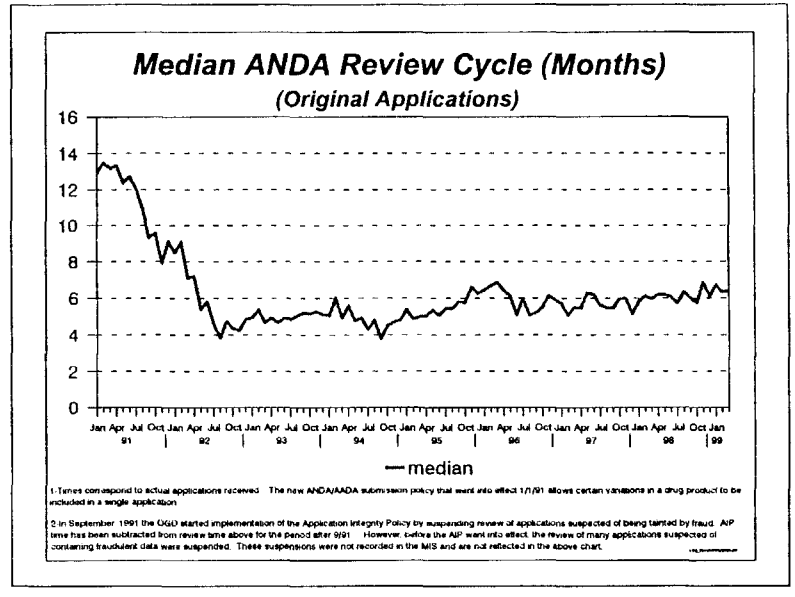


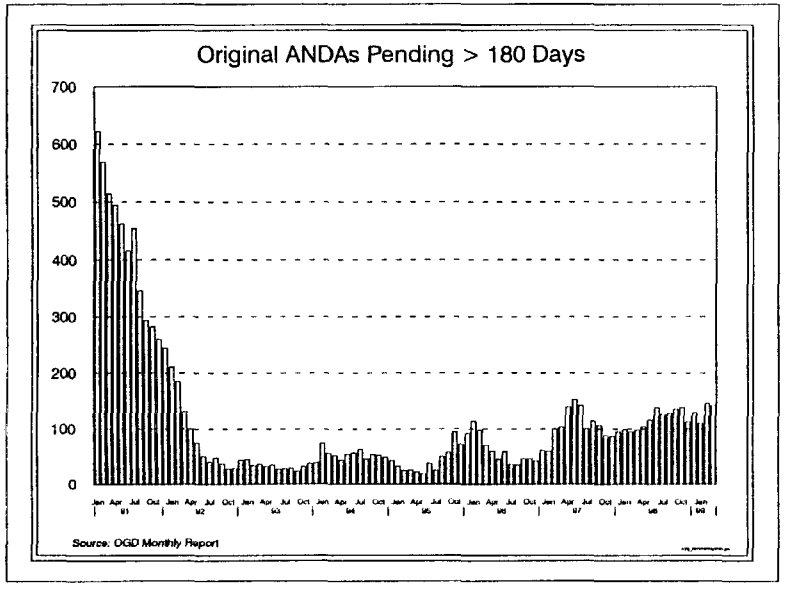
1-Times correspond to actual applications received. The new ANDA/AADA submission policy that went into effect 1/1/91 allows certain variations in a drug product to be included in a single application.

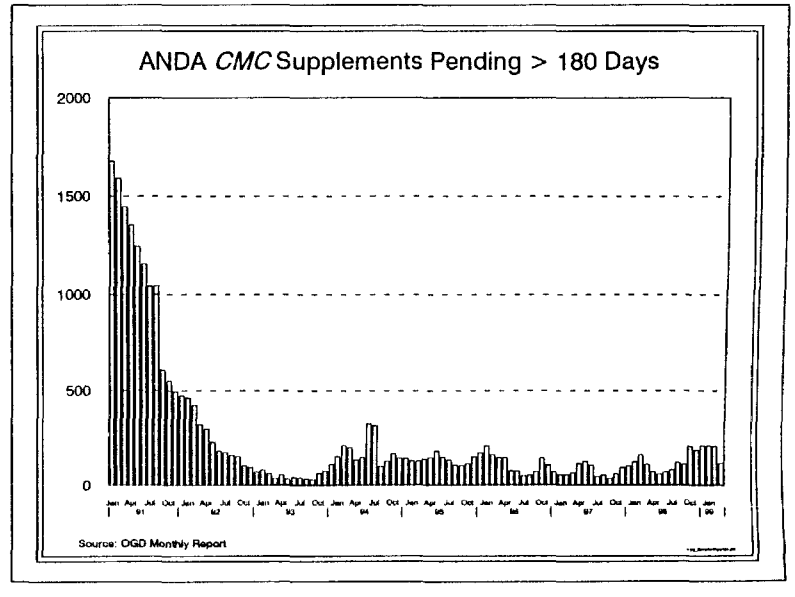
2-In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. AIP time has been subtracted from review time above for the period after 9/91. However, before the AIP went into effect, the review of many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

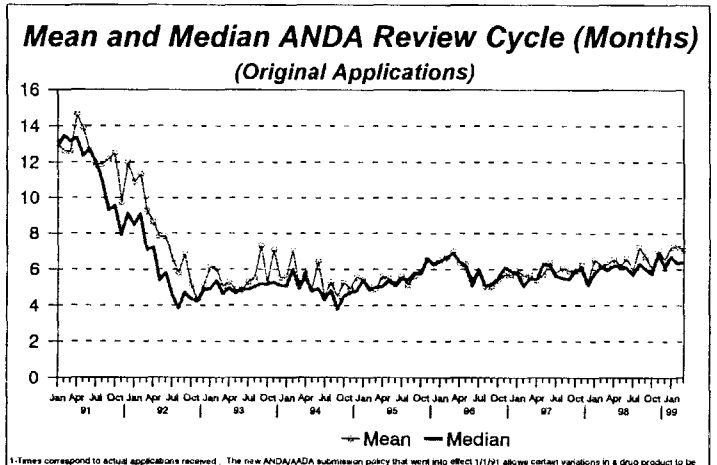
Note: Global Supplements Collapsed


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
91 92 93 94 95 96 97 98 99
Status as of April 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
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



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.

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1.	75-010	IBUPROFEN TABLETS, USP (ROUND & CAPSULE-SHAPED, BROWN) (OTC) 200 MG	LNK INTERNATIONAL, INC.	03/01/99
2.	75-139	IBUPROFEN TABLETS, USP (ROUND & CAPSULE-SHAPED, WHITE) (OTC) 200 MG	LNK INTERNATIONAL. INC.	03/01/99
3.	75-351	BUTALBITAL, ASPIRIN, CAFFEINE, AND CODEINE PHOSPHATE CAPSULE 50 MG/325 MG/40 MG/30 MG	ENDO PHARMACEUTICALS, INC.	03/05/99
4.	40-305	MEPERIDINE HYDROCHLORIDE INJECTION, USP (PRESERVATIVE-FREE) 10 MG/ML	FAULDING PHARMACEUTICAL CO.	03/10/99
* 5.	74-507	NICOTINE POLACRILEX GUM, USP (OTC) 2 MG (BASE)	CIRCA PHARMACEUTICALS, INC.	03/15/99
6.	40-203	OXYCODONE AND ACETAMINOPHEN TABLETS, USP 5 MG/325 MG	AMIDE PHARMACEUTICAL, INC.	03/15/99
7.	40-289	OXYCODONE AND ACETAMINOPHEN CAPSULES, USP 5 MG/500 MG	DURAMED PHARMACEUTICALS, INC.	03/16/99
* 8.	74-707	NICOTINE POLACRILEX GUM, USP (OTC) 4 MG (BASE)	CIRCA PHARMACEUTICALS, INC.	03/19/99
9.	65-005	MINOCYCLINE HYDROCHLORIDE CAPSULES, USP 50 MG (BASE), 100 MG (BASE)	GLOBAL PHARMACEUTICAL CORPORATION	03/23/99
* 10.	75-270	KETOPROFEN EXTENDED-RELEASE CAPSULES 100 MG, 150 MG, 200 MG	ANDRX PHARMACEUTICALS, INC.	03/24/99
11.	75-327	LEUCOVORIN CALCIUM TABLETS, USP 15 MG (BASE)	INVAMED INC,	03/24/99
12.	40-291	FLUOROURACIL INJECTION, USP 250 MG/5 ML, 500 MG/10 ML	BIGMAR, INC.	03/24/99
13.	74-723	DICLOFENAC SODIUM DELAYED-RELEASE TABLETS, USP 50 MG	NOVOPHARM LTD.	03/30/99
14.	75-262	ALBUTEROL SULFATE SYRUP 2 MG (BASE)/5 ML	UDL LABORATORIES	03/30/99
15.	74-962	PENTOXIPHYLLINE EXTENDED-RELEASE TABLETS 400 MG	UPSHER SMITH LABORATORIES, INC.	03/31/99

NOTE: Under item 10, the 200 mg strength has previously been approved for another applicant. Thus, only the 100 mg and 150 mg strengths represent first-generic approvals.

1.	75-048	ENALAPRIL MALEATE TABLETS, USP 2.5 MG, 5 MG, 10 MG, 20 MG	GENEVA PHARMACEUTICALS, INC.	03/05/99
2.	75-254	RANITIDINE TABLETS, USP (OTC) 75 MG	RANBAXY PHARMACEUTICALS, INC.	03/10/99
3.	75-108	NIFEDIPINE EXTENDED-RELEASE TABLETS 30 MG	MYLAN PHARMACEUTICALS, INC.	03/15/99
4.	74-876	CIPROFLOXACIN TABLETS, USP 250 MG, 500 MG, 750 MG	NOVOPHARM LIMITED	03/24/99
5.	75-277	ENALAPRIL MALEATE TABLETS, USP 2.5 MG, 5 MG, 10 MG, 20 MG	ESI LEDERLE, INC.	03/29/99