GAO

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Health, Education and Human Services Division

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June 3, 1997

The Honorable James M. Jeffords
Chairman
The Honorable Edward M. Kennedy
Ranking Minority Member
Committee on Labor and Human Resources
United States Senate

Subject: Medical Devices: FDA Review Times, 1989 Through 1996

The Food and Drug Administration (FDA) regulates the manufacture and marketing of tens of thousands of medical devices in this country. This regulatory function is carried out in a number of ways, perhaps the most important of which is the review of submissions from manufacturers wishing to market medical devices for the first time. Device manufacturers have admonished FDA for taking too much time to conduct these reviews and have argued that the agency's review imposes inordinate delays upon the introduction of new devices into the market. FDA, while admitting that device review times were lengthy, responded that it has made considerable gains recently in improving the timeliness of reviews.

We issued a report on medical device review times in 1995 that addressed this issue.[1] We found that review times for the most prevalent type of device submissions had lengthened throughout the early part of the decade but had improved slightly in 1994. FDA maintained that the increases in review time for submissions from 1990 through 1993 created a backlog of thousands of cases. The decrease in review time between 1993 and 1994 was portrayed as evidence that FDA had succeeded in cleaning up this backlog.

Critics of FDA had a very different interpretation of the data in our 1995 report. These data, they said, showed increases in review times for each year with only

[1]Medical Devices: FDA Review Time (GAO/PEMD-96-2, Oct. 30, 1995).

one exception. Furthermore, it would be difficult to use the 1 year in which review times decreased (1994) as evidence of any positive trend.

Data on review times beyond the 1994 date would be helpful for resolving the question of whether the downturn in that year was a one-time event or indicated that agency performance was truly improving. Therefore, at your request we have measured review times for medical device submissions to FDA in fiscal years 1995 and 1996.[2] We present our results along with those for submissions between 1989 and 1994 in order to show the trends in review times.

Our examination focused on the three major types of device submissions received by FDA:

- Premarket notifications or 510(k)s[3]–These are notifications to FDA of a manufacturer's intent to market a device that the manufacturer considers substantially equivalent to a device already on the market. In evaluating 510(k) notifications, FDA makes a determination whether the new device is substantially equivalent to a legally marketed device.

- Premarket approval (PMA) applications–These are applications requesting FDA approval to market a medical device. A PMA is needed when the risks associated with a device are considerable (as would be the case, if the device is implanted in the body for life-supporting purposes, such as a defibrillator) or when the device is new (and therefore, the risks are not well understood).

- PMA supplements–These are applications to modify a device originally approved through the PMA process in some way that may affect the safety or effectiveness of that device. Such modifications include new uses for the device, device design, materials used in constructing the device, quality control procedures used in manufacturing, or a change in the manufacturing facility or the packaging for the device.

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[2]All references in this report are to fiscal years. The federal fiscal year begins on Oct. 1 and ends on Sept. 30.

[3]Premarket notification is commonly called 510(k) in reference to section 510(k) of the Federal Food, Drug, and Cosmetic Act.

We obtained data for all the notifications and applications in these three categories received by FDA from the beginning of 1989 through March 31, 1997.[4] Our primary measure of time was the interval between FDA's receipt of an application and the "final decision" made on that application. Alternative measures of time were also calculated and are included in our analysis. We deleted cases that had missing values or apparent data entry errors for the values relevant to calculating review time.

Because the validity of FDA's raw data on review times has not been questioned even by critics of the review process, we did not, for this or our earlier review, verify those data. With this exception, we performed our work between March and May 1997 in accordance with generally accepted government auditing standards.

RESULTS IN BRIEF

The trends in review times for premarket notifications, original PMAs,[5] and PMA supplements submitted from 1989 through 1996 are strikingly similar. As figures 1 through 3 show, the decrease in review times that began in 1994 continued in 1995 and 1996 for each of these types of submissions.

[4]Because 1997 notifications and applications are still being received and reviewed, our results on review times are presented only for submissions through the end of fiscal year 1996.

[5]The term "original PMA" is used to distinguish this type of application from a PMA supplement.

Figure 1: Median Review Time for 510(k)s by Fiscal Year

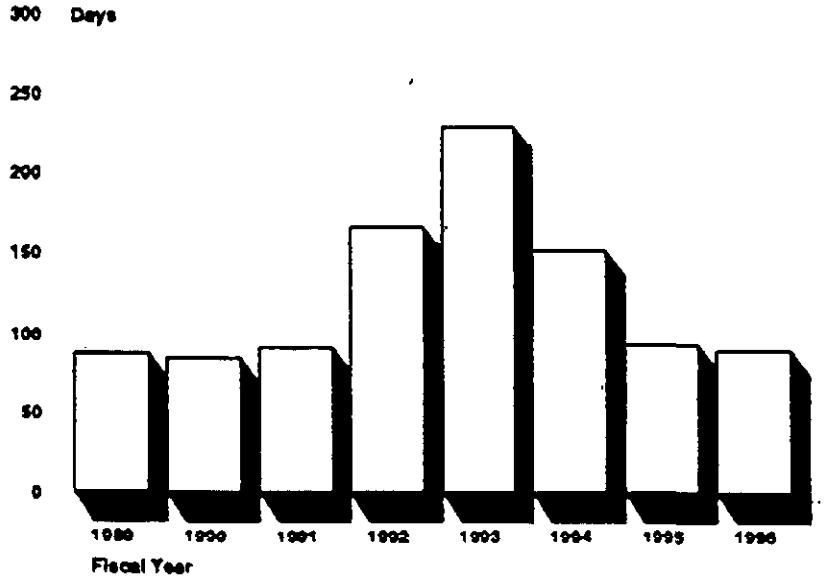


Figure 2: Median Review Time for Original PMAs by Fiscal Year

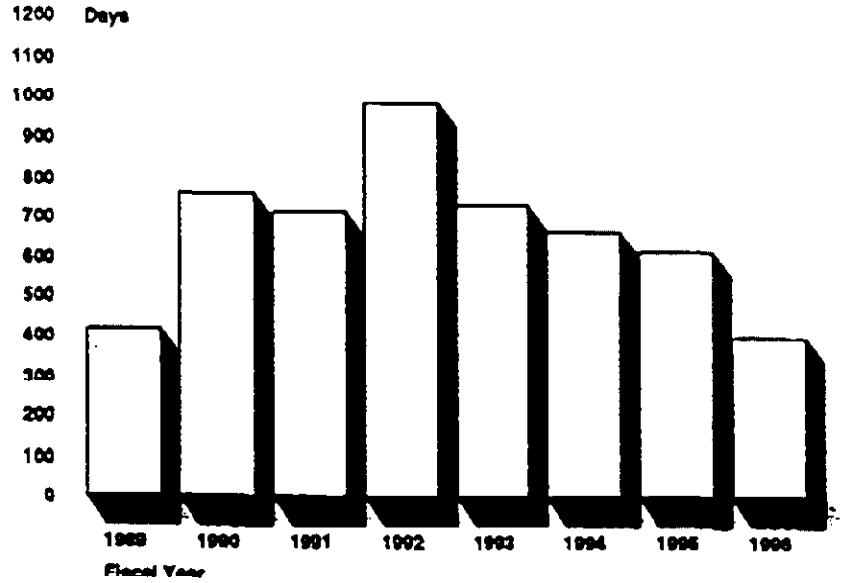
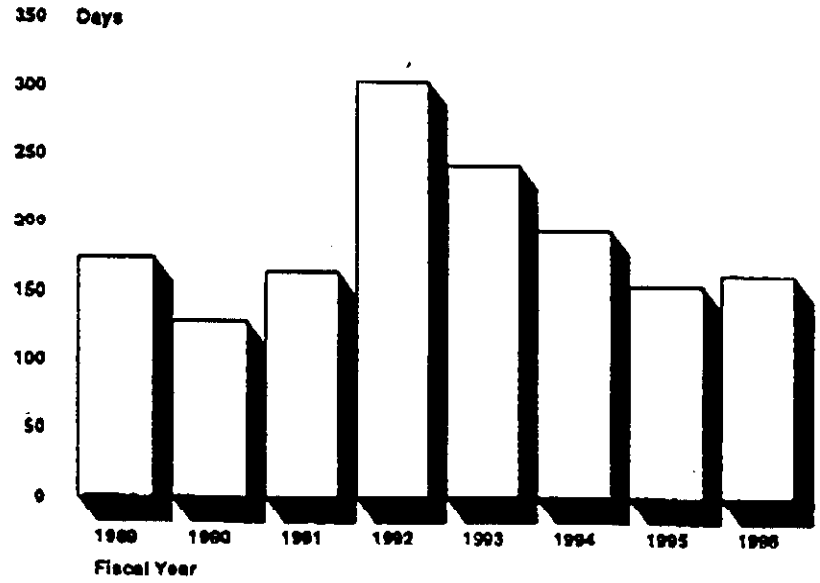


Figure 3: Median Review Time for PMA Supplements by Fiscal Year



The pattern in review times in each of the figures is consistent with FDA's claims that the increases early in the period reflected a growing backlog of applications and notifications and that the improvements in the later years indicated that this backlog had been successfully cleared.

At the same time, despite the overall positive trend in these results, it should be noted that between 1995 and 1996 the review time for PMA supplements increased slightly. Despite this increase, the median review time for 1996 PMA supplements remains shorter than for those submitted in 1994. Thus, it is not clear whether this is the start of a new trend of increasing review times or a single exception to the overall positive trend seen since 1992.

GAO ANALYSIS

In figures 1 through 3, we used the median as the measure of "typicality" and show the median for all submissions to FDA, irrespective of FDA's ultimate determinations. We relied on the median because it is acknowledged to be the preferred measure of central tendency in situations where there are extreme values (as is the case with device review times). We included all submissions

because even those that were never approved required FDA resources for review. In the tables that follow, however, we present some alternative measures of review time. We also present some basic descriptive information on the medical device submissions.

Tables 1, 3, and 5 show the number of 510(k)s, original PMAs, and PMA supplements, respectively, that were submitted to FDA. Each table also shows the disposition of those submissions. Tables 2, 4, and 6 show the average (or "mean") review times for 510(k)s, original PMAs, and PMA supplements, respectively. We present average review times for each type of submission because this statistic has been frequently reported and to show that the trends remain the same notwithstanding the measure that is used. The data in these tables also differ from those in figures 1 through 3 in that (1) they are restricted to submissions that were eventually cleared or approved, and (2) they distinguish between average "FDA time" (the amount of time the application was under active review by the agency) and average "non-FDA time" (any time that the sponsor of the application took to respond to inquiries from FDA for additional information).

Premarket Notifications (510(k)s)

FDA does not approve 510(k) notifications. Rather, the agency makes a determination of whether the device is substantially equivalent to devices already on the market. If so, the manufacturer can market the new device. Table 1 shows the number of 510(k) notifications submitted to FDA from 1989 through 1997 and the disposition of those notifications. Table 2 shows review times for those 510(k) submissions judged to be "equivalent."

Table 1: Disposition of 510(k) Notification Submitted, 1989-97

Fiscal year submitted	Judged equivalent	Judged nonequivalent	Other[a]	Open	Total
1989	5,258	108	1,657	0	7,023
1990	4,631	142	1,062	0	5,835
1991	4,513	146	1,114	1	5,774
1992	4,912	202	1,409	10	6,533
1993	4,752	109	1,428	21	6,310
1994	4,827	96	1,500	27	6,450
1995	4,789	71	1,153	65	6,078
1996	4,073	43	662	538	5,316
1997[b]	967	8	172	1,360	2,507
Total	**38,722**	**925**	**10,157**	**2,022**	**51,826**

[a]The "Other" category includes the following FDA disposition codes: additional information requested, applicant cannot respond within 30 days; forwarded to drugs/biologics; deleted/duplicate; deleted; drug (CDER) review required; exempted by regulation; general purpose article; closeout letter issued; not actively regulated; not a device; not a finished product; not a required submission; preamendment exempt; refuse to accept; reconditioner/remanufacturer; transitional device; and withdrawn by applicant.

[b]Through Mar. 31, 1997.

Table 2: Review Time (in Days) for 510(k) Notifications Judged to Be Equivalent

Fiscal year submitted	Median total time	Average total time	Average FDA time	Average non-FDA time
1989	78	98	77	21
1990	78	100	80	21
1991	88	124	96	28
1992	142	209	169	41
1993	199	247	207	40
1994	125	177	134	44
1995	89	126	99	27
1996	85	109	89	19

As can be seen from table 2, the pattern of increases in review times during the early years followed by decreasing times that was seen for all 510(k) notifications combined also held for each measure in the group of notifications that were eventually cleared for marketing. Moreover, the data are also consistent across measures in that times for the 1996 cohort remained longer than for the 1989 cohort.

Original Premarket Approvals (PMAs)

To market a "new" device (that is, one that is not substantially equivalent to a device already on the market) or a device that is seen as having considerable risks, a manufacturer must submit an application to FDA seeking premarket approval. The number of original PMAs submitted is considerably less than the number of 510(k) applications. However, because FDA reviews a substantial amount of evidence to determine if these devices are safe and effective (unlike with 510(k)s where the principal concern is whether they are substantially equivalent), original PMAs typically require considerably more resources for review than do 510(k)s. Table 3 shows the number of original PMAs submitted to FDA from 1989 through 1997 and the disposition of those applications. Table 4 shows review times for original PMA submissions approved.

Table 3: Disposition of Original PMA Applications Submitted, 1989-97

Fiscal year submitted	Approved	Withdrawn	Other[a]	Open	Total
1989	46	28	10	0	84
1990	38	28	10	2	78
1991	21	31	13	7	72
1992	33	21	8	4	66
1993	15	21	3	1	40
1994	21	9	1	11	42
1995	17	7	1	15	40
1996	12	6	5	21	44
1997[b]	1	0	1	27	29
Total	**204**	**151**	**52**	**88**	**495**

[a]The "Other" category includes the following FDA disposition codes: abandoned; converted; reclassified; PMA not appropriate; and other.

[b]Through Mar. 31, 1997.

Table 4: Review Times (in Days) for Approved Original PMAs

Fiscal year submitted	Median total time	Average total time	Average FDA time	Average non-FDA time
1989	355	454	321	133
1990	531	788	541	247
1991	722	712	483	229
1992	907	1,016	667	349
1993	766	777	534	243
1994	623	600	452	148
1995	417	428	362	66
1996[a]	280	271	235	36

[a]The median and average approval times for the 1996 PMA submissions will increase as applications currently open are approved.

As can be seen from table 4, the pattern of increases in review times during the early years followed by decreasing times that was seen for all PMA submissions also held for each measure in the group of applications that were eventually approved for marketing.

PMA Supplements

Table 5 shows what happened to applications in the third category of medical device submissions that we examined, supplements to devices originally approved as PMAs. Table 6 presents review times for these approved applications.

Table 5: Disposition PMA Supplements Submitted, 1989-97

Fiscal year submitted	Approved	Withdrawn	Other[a]	Open	Total
1989	642	138	27	0	807
1990	559	75	25	1	660
1991	500	75	17	4	596
1992	478	105	21	3	607
1993	326	44	23	2	395
1994	315	42	9	6	372
1995	443	33	7	10	493
1996	323	17	5	66	411
1997[b]	85	5	0	130	220
Total	**3,671**	**534**	**134**	**222**	**4,561**

[a]The "Other" category includes the following FDA disposition codes: abandoned; converted; reclassified; PMA not appropriate; and other.

[b]Through Mar. 31, 1997.

Table 6: Review Time (in Days) for Approved PMA Supplements

Fiscal year submitted	Median total time	Average total time	Average FDA time	Average non-FDA time
1989	160	190	157	33
1990	116	170	132	38
1991	140	240	169	71
1992	215	317	260	57
1993	215	277	234	43
1994	180	223	179	44
1995	142	171	139	32
1996[a]	127	133	122	11

[a]The median and average approval times for the 1996 PMA supplements will increase as applications currently open are approved.

As can be seen from table 6, the pattern for review time for PMA supplements parallels that for the other submissions we examined. That is, times increased throughout the early years (1989 through 1993) and then decreased quickly through 1996.

AGENCY COMMENTS

We provided a draft of this letter to FDA. They agreed with our finding that review times had decreased since 1993. In addition, FDA provided a number of technical comments that have been incorporated into the text.

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As agreed with your office, we will send copies of this letter to other interested congressional committees, the Secretary of Health and Human Services, and the Commissioner of Food and Drugs. Copies will also be made available to others upon request.

This letter was prepared by Bertha Dong and George Silberman. If you or your staff have any questions about this report, please call me at (202) 512-6543 or you may call Ms. Dong at (202) 512-8499 or Mr. Silberman at (202) 512-9226.

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and Public Health Issues

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