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August 2004

FOOD AND DRUG ADMINISTRATION

Data to Measure the Timeliness of Reviews of Medical Device Applications Are Limited

GAO-04-1022

August 2004

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Data to Measure the Timeliness of Reviews of Medical Device Applications Are Limited

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Highlights

Highlights of GAO-04-1022, a report to congressional committees

Why GAO Did This Study

FDA reviews applications from manufacturers that wish to market medical devices in the United States. To ensure prompt approval of new devices and clearance of devices that are substantially equivalent to those legally on the market, the Congress passed the Medical Device User Fee and Modernization Act of 2002 (MDUFMA). The act authorizes FDA to collect user fees and, in return, requires FDA to meet performance goals that are tied to the agency's review process. The goals set actions FDA may take on applications and specify the time that FDA should take in certain phases of the review process.

MDUFMA requires GAO to report on FDA's performance against the MDUFMA performance goals established for fiscal years 2003 and 2004 and to determine whether FDA is likely to meet the fiscal year 2005 performance goals. MDUFMA also requires GAO to report on the amounts FDA obligated in fiscal year 2002 for medical device compliance activities and inspections of manufacturers after their devices are marketed.

GAO analyzed data provided by FDA that are based on actions taken on applications FDA received from October 1, 2002, through March 31, 2004. GAO also analyzed data on the amounts FDA obligated for medical device compliance and inspection activities for fiscal year 2002.

www.gao.gov/cgi-bin/getrpt?GAO-04-1022.

To view the full product, including the scope and methodology, click on the link above. For more information, contact Marcia Crosse at (202) 512-7119.

What GAO Found

FDA had limited data that could be used to measure the agency's performance against most of the MDUFMA performance goals. Thus, it is uncertain whether FDA will meet the MDUFMA performance goals for fiscal years 2003, 2004, and 2005. For fiscal years 2003 and 2004, there were two performance goals in effect for each year. As of March 31, 2004, only one application was subject to the action tied to one of the two MDUFMA performance goals. On this application, FDA completed its review and made the decision to approve the application within the goal's established time frame. To determine the likelihood of meeting the 20 MDUFMA performance goals for fiscal year 2005, FDA is collecting data on its performance against these goals. GAO found that FDA had performance data for some, but not all, of the MDUFMA performance goals. From fiscal year 2003 applications, data were available to compare FDA's performance against 17 of the 20 fiscal year 2005 performance goals. FDA took actions tied to 14 of the 17 goals within the goals' established time frames. From fiscal year 2004 applications, data were available to compare FDA's performance against 11 of the 20 performance goals. FDA took actions tied to the 11 goals within the goals' established time frames. The results of FDA's performance against MDUFMA performance goals are preliminary, however, because 8 percent and 49 percent, respectively, of the applications FDA accepted in fiscal year 2003 and the first 6 months of fiscal year 2004 were awaiting action by FDA or responses from manufacturers. Because FDA's performance against the MDUFMA performance goals is based on the percentages of actions the agency takes within required review times, FDA's results could change as the agency completes its actions on all applications for which the goals apply.

FDA obligated about $128 million for postmarket medical device compliance activities and inspections in fiscal year 2002. FDA obligated about $109 million for compliance activities for outreach coordination, such as guidance to field staff on reporting problems with medical devices, laboratory analyses, and research, such as the development of domestic and international standards to provide reasonable assurance that medical device products are safe and effective. FDA obligated about $19 million for inspections of device manufacturers' establishments, including routine surveillance inspections to determine compliance with medical device regulations and inspections resulting from device problem reporting or product recalls.

In commenting on a draft of this report, FDA generally agreed with its findings.

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Abbreviations

BLA	biologics license application
CBER	Center for Biologics Evaluation and Research
CDRH	Center for Devices and Radiological Health
FDA	Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetics Act
GMP	good manufacturing practices
HHS	Department of Health and Human Services
MDUFMA	Medical Device User Fee and Modernization Act of 2002
PMA	premarket approval

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United States Government Accountability Office
Washington, D.C. 20548

August 30, 2004

The Honorable Judd Gregg
Chairman
The Honorable Edward M. Kennedy
Ranking Minority Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Joe Barton
Chairman
The Honorable John D. Dingell
Ranking Minority Member
Committee on Energy and Commerce
House of Representatives

The Food and Drug Administration (FDA) is responsible for regulating medical devices—such as tongue depressors, pacemakers, and artificial hearts—to provide reasonable assurance of their safety and effectiveness for human use. As part of its regulatory responsibilities, FDA reviews applications from manufacturers that wish to have their new medical devices or devices substantially equivalent to those already on the market approved for marketing in the United States. When required, FDA inspects manufacturers' establishments prior to approval. FDA is also responsible for implementing and enforcing medical device regulations related to compliance activities, which include the reporting of problems associated with the safety and effectiveness of devices and inspections of manufacturers' device establishments after devices reach the market.

Each year FDA receives approximately 10,000 medical device applications. Members of the Congress, representatives of the medical device industry, and others have expressed concern about the length of time it takes FDA to review applications for marketing medical devices, with the consequence of possibly delaying patients' access to useful, and possibly life-saving, medical devices.

In October 2002, the Congress passed the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) to provide FDA with additional

resources to ensure prompt approval or clearance[1] of applications for marketing medical devices and licensing biological products.[2] MDUFMA authorized FDA to collect user fees from manufacturers that submit several types of applications to FDA for marketing medical devices. In return, MDUFMA requires FDA to meet performance goals tied to the review process for medical device and biological applications. MDUFMA also requires the Secretary of Health and Human Services (HHS) to develop the specific goals FDA must meet. The Secretary developed performance goals for fiscal years 2003 through 2007. These MDUFMA performance goals are set for certain actions FDA may take during the application review process and specify lengths of time for taking these actions. FDA's performance against the MDUFMA performance goals is based on the percentages of actions the agency takes on applications within required review times. To help FDA meet the MDUFMA performance goals, the Secretary of HHS also identified several goal-related activities for FDA to undertake, such as hiring additional review staff.

The number of MDUFMA performance goals that FDA must meet increases over time. For fiscal years 2003 and 2004, FDA must meet the same two performance goals for each year. For example, one of the performance goals requires FDA to review a manufacturer's response to the agency's request for additional information on applications that are approvable with minor corrections or clarifications,[3] and then take the next appropriate action, such as make a decision to approve the application. To meet the performance goal, FDA must review and make the decision within 30 days on 90 percent of the applications received for each fiscal year. In fiscal year 2005, FDA must meet the two goals and an additional 18 performance goals tied to medical device and biological product applications, for a total of 20. The 20 performance goals are tied to times for reviews, decisions, or a combination of both.

MDUFMA requires us to report on FDA's performance as measured against the fiscal years 2003 and 2004 MDUFMA performance goals and determine

[1]The term "approval" is generally used for applications for new devices, while the term "clearance" is used for devices that are substantially equivalent to those legally on the market.

[2]Pub. L. No. 107-250, 116 Stat. 1588.

[3]FDA's request for additional information on such applications is known as an "approvable" letter.

whether the agency is likely to meet the fiscal year 2005 MDUFMA performance goals. MDUFMA also requires us to report on the amounts FDA obligated in fiscal year 2002 for medical device compliance activities and inspections of manufacturers' device establishments after their devices are marketed, excluding the amounts that were obligated for inspections related to the review of medical device applications.

To examine FDA's performance, we analyzed actions taken by FDA on applications that it received from fiscal year 2003 through the first 6 months of fiscal year 2004 (October 1, 2003, through March 31, 2004). At the time of our review, performance data through March 31, 2004, were the most current FDA data available. To assess FDA's performance against the two MDUFMA performance goals that were established for fiscal years 2003 and 2004, we analyzed performance data for applications received in those years. To determine the likelihood of FDA meeting its fiscal year 2005 MDUFMA performance goals, we compared performance data that FDA is collecting on fiscal years 2003 and 2004 applications to the 20 MDUFMA performance goals that will be effective in fiscal year 2005. We also reviewed relevant documents and interviewed officials from FDA's Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER) about two key FDA medical device application review processes and the agency's performance as measured against the MDUFMA performance goals. These two processes are referred to as (1) the Premarket Approval (PMA) review process, which is used to review an application for a new medical device or when the risks associated with the device are considerable, and (2) the 510(k) review process, which is used to review an application for a type of device that may be substantially equivalent to one already on the market. In addition, we reviewed documentation of FDA's procedures for checking the reliability of MDUFMA performance data and met with FDA officials to discuss their efforts to verify the accuracy and consistency of their reported performance data. We determined that the performance data were sufficiently reliable for the purposes of this report.

To determine the amounts FDA obligated in fiscal year 2002 for medical device compliance activities and inspections of manufacturers' device establishments after devices are marketed, we reviewed and analyzed data from FDA's fiscal year 2004 budget justification and information FDA provided related to these data. The fiscal year 2004 budget justification contains FDA's fiscal year 2002 actual obligations for medical device compliance activities and inspections. To assess the reliability of these data, we reviewed supporting documentation that FDA provided on the

obligations reported in the agency's fiscal year 2004 budget justification related to compliance activities and inspections for marketed devices. We also reviewed FDA's fiscal year 2003 audited financial statement report that contained information about the reliability of fiscal year 2002 obligations data. The review found no material weaknesses related to our work. Based on these reviews, we determined that the obligations data were sufficiently reliable for the purposes of this report. We conducted our work from January 2004 through August 2004 in accordance with generally accepted government auditing standards.

Results in Brief

FDA had limited data that could be used to measure the agency's performance against most of the MDUFMA performance goals. Thus, it is uncertain whether FDA will meet the goals established for fiscal years 2003, 2004, and 2005. For example, for fiscal year 2003, the two performance goals could be applied to 53 applications. However, as of March 31, 2004, only one application was subject to a review and a decision tied to one of the two MDUFMA performance goals. On that application, FDA reviewed the manufacturer's complete response to FDA's approvable letter and made the decision to approve the application within the goal's established time frame. For fiscal year 2004, there was no application subject to the review and decision tied to the two fiscal year 2004 MDUFMA performance goals. FDA had performance data for some, but not all, of the MDUFMA performance goals that will be effective in fiscal year 2005. For applications received in fiscal year 2003, data were available to compare FDA's performance against 17 of the 20 performance goals for fiscal year 2005. FDA took actions on applications tied to 14 of the 17 performance goals within the established time frames. For fiscal year 2004 applications, FDA had performance data for 11 of the 20 performance goals. FDA took actions on applications tied to the 11 goals within the established time frames. The results of FDA's performance against MDUFMA goals are preliminary, however, because many of the applications FDA received in fiscal year 2003 and the first 6 months of fiscal year 2004 were pending within the review process. Because FDA's performance against the MDUFMA performance goals is based on the percentages of actions the agency takes on applications within required review times, FDA's performance results could change as the agency completes actions on all applications for which the performance goals apply.

FDA obligated over $128 million for postmarket medical device compliance activities and inspections in fiscal year 2002. FDA obligated about

$109 million for compliance activities for outreach coordination, such as guidance to field staff on the reporting of problems with medical devices; laboratory analyses; and research, such as the development of domestic and international standards to help provide reasonable assurance that medical devices are safe and effective. FDA obligated about $19 million for inspections of manufacturers' device establishments that included routine surveillance inspections to determine compliance with medical device regulations and inspections resulting from device problem reporting or product recalls.

We provided a draft of this report to FDA, which generally agreed with its findings. FDA believes that it has made a good start in its implementation of MDUFMA and believes its progress with the MDUFMA performance goals is consistent with the extensive performance improvements the agency is expected to achieve each year through 2007.

Background

Under the Federal Food, Drug, and Cosmetic Act (FDCA),[4] FDA is responsible for ensuring that medical devices are reasonably safe and effective before they go to market (premarket) and that marketed device products remain safe (postmarket). Two FDA centers, CDRH and CBER, are responsible for the PMA and clearance of medical device applications.[5] CDRH reviews applications for the majority of devices marketed, such as artificial hearts, dialysis machines, and radiological devices. CBER reviews applications for devices used in the testing and manufacture of biological products, such as diagnostic tests intended to screen blood donors (such as for the human immunodeficiency virus), as well as devices used in cell and gene therapies.

Each fiscal year, FDA obligates funds for postmarket compliance activities and inspections related to medical devices and radiological products. FDA provides field staff with guidance on inspecting manufacturers' establishments after devices have been marketed, for compliance with the good manufacturing practices (GMP) requirements, monitoring

[4]Ch. 675, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301 et seq. (2000)).

[5]In general, medical device applications for PMA that are reviewed by FDA include information on the device and its components; proposed labeling for the device; and when applicable, clinical and nonclinical studies that provide reasonable assurance of the device's safety and effectiveness.

manufacturers' corrections of problems with devices, and removing unsafe devices from the market. FDA has 21 district offices that support inspections of manufacturers' establishments. During inspections for compliance with GMP requirements, FDA investigators examine manufacturer facilities, records of manufacturing processes, and corrective action programs.

Types of Applications Reviewed under MDUFMA Performance Goals

MDUFMA identified eight types of applications for medical devices and biological products that are subject to the performance goals developed by the Secretary of HHS for fiscal years 2003, 2004, and 2005:

- Original PMA applications are generally required when the device is new or when the risks associated with the device are considerable (as would be the case if the device is implanted in the body for life-supporting purposes).

- Premarket Notifications, or 510(k)s,[6] are applications used when the intent is to market a type of device that may be considered substantially equivalent[7] to one already on the market and therefore, does not require PMA.

- Premarket Reports are applications required for high-risk devices originally approved for a single use that a manufacturer has reprocessed for additional uses.

- Panel-Track Supplements are applications used to supplement approved PMAs or Premarket Reports. These supplements typically request approval of a significant change in the design or performance of a device, or for a new purpose for using the device.

- Expedited Original PMAs are used when a manufacturer seeks priority status to market a medical device that is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition or to address an unmet medical need.

[6]FDA uses the term 510(k) to refer to a premarket notification submission.

[7]Substantial equivalence means that a device has (1) the same intended use and same technological characteristics as a marketed device or (2) the same intended use and different technological characteristics but is as safe and effective as the marketed device and does not raise new questions of safety and effectiveness.

- The 180-day PMA Supplements are used to supplement approved PMAs or premarket reports. The application typically requests approval of a significant change in aspects of a device, such as its design, specifications, or labeling.

- Biologics license applications (BLAs)[8] Resubmissions (Class 1) are used to respond to information requested by FDA on a BLA and may include matters related to product labeling or safety and other minor clarifying information.

- BLA Supplement Resubmissions (Class 2) are used to respond to an FDA request for information on a BLA regarding the safety and effectiveness of products or a re-inspection of the manufacturer's device establishment.

FDA's Medical Device Application Review Processes

FDA primarily uses two medical device application review processes; the PMA review process and the 510(k) review process.[9] FDA annually receives about 50 PMAs and about 4,000 510(k) applications for review through these processes.

The PMA Review Process

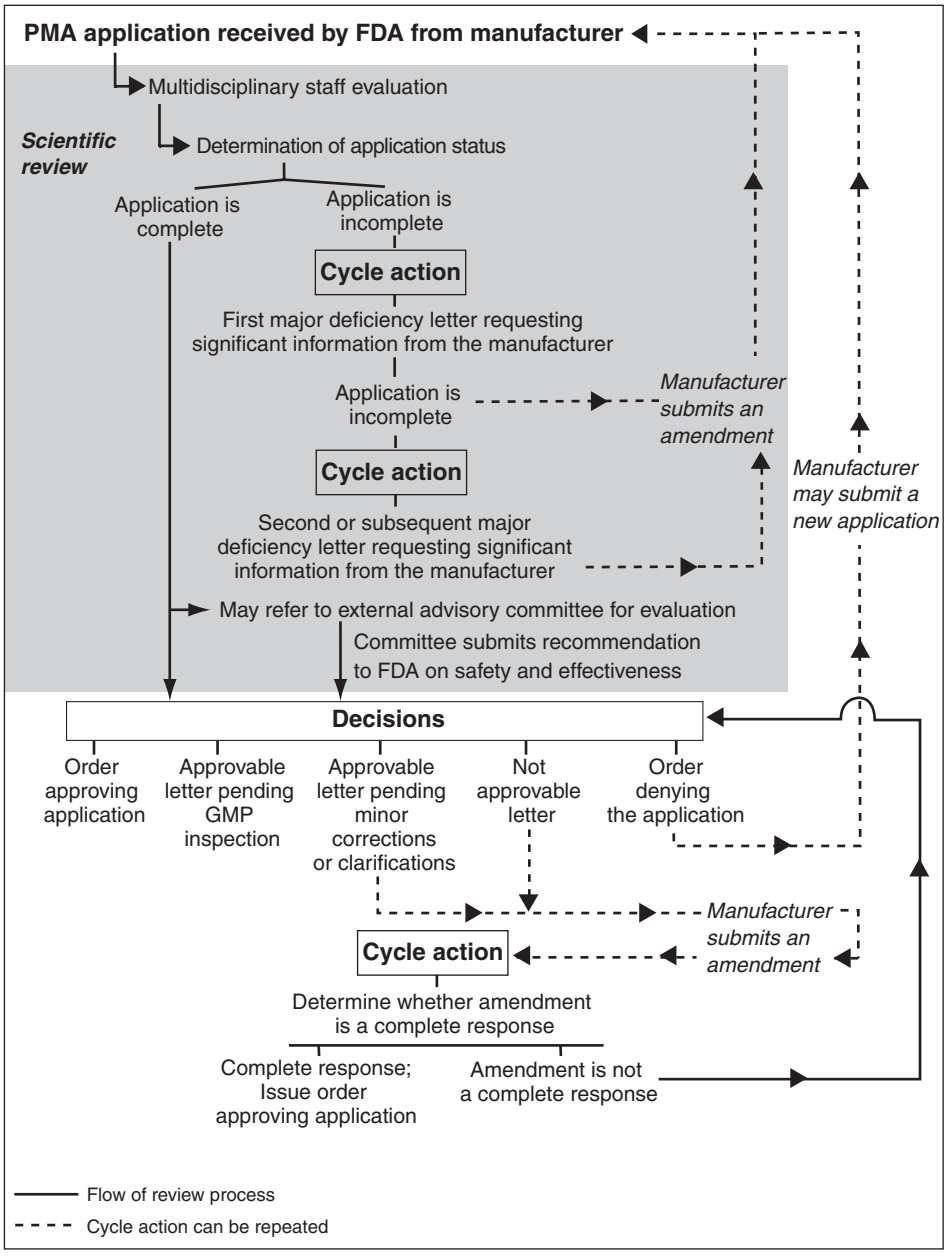
Under the PMA review process, FDA reviews applications for new devices or those for which risks associated with the device are considerable. Applications reviewed under this process include Original PMAs, Premarket Reports, Panel-Track Supplements, Expedited Original PMAs, and 180-day PMA Supplements. After an initial screening of an application and determination that the review should proceed, an FDA multidisciplinary staff conducts a scientific review of the application[10] and determines whether it is complete, that is, if it contains sufficient information to allow the review to continue. (See fig. 1.)

[8]BLAs are used to request permission to introduce and license biological products into interstate commerce.

[9]According to FDA officials, BLA applications go through a review process that is similar to the PMA review process.

[10]The scientific review can include reviews of results from clinical investigations of the device that involve human subjects. FDA also reviews nonclinical studies of the device, studies that may include microbiological, toxicological, and engineering tests.

Figure 1: PMA Review Process



Source: GAO.

For complete applications, FDA may make one of five decisions. FDA may (1) issue an order approving the application, which allows the manufacturer to begin marketing the device; (2) send the manufacturer an approvable letter pending a GMP inspection, which indicates that FDA should be able to approve the device after the agency finds that the manufacturer's device establishment is in compliance with GMP requirements; (3) send the manufacturer an approvable letter indicating that the agency should be able to approve the device if the manufacturer can make minor corrections or clarifications to the application; (4) issue a "not approvable" letter informing the manufacturer that FDA does not believe that the application can be approved because the data provided by the manufacturer do not demonstrate that the device is reasonably safe and effective; or (5) issue an order denying approval of the application, which informs the manufacturer that the agency has completed its scientific review, identified major safety and effectiveness problems, and decided not to approve the application. FDA may refer complete applications to an external advisory committee for evaluation when a device is the first of its kind or when the agency believes it would be useful to have independent expertise and technical assistance to properly evaluate the safety and effectiveness of the device.[11] For applications referred to an advisory committee, the committee submits recommendations to FDA on the safety and effectiveness of the devices. Taking the committee's recommendations into consideration, FDA then makes its decision.

For incomplete applications, that is, applications for which FDA determines it needs significant additional information, FDA issues a "major deficiency letter" to the manufacturer identifying the information that is required to provide reasonable assurance of the safety and effectiveness of the device. This request for significant information is an action referred to as a cycle action. In general, FDA takes cycle actions when it requests additional information from the manufacturer, or when it evaluates additional information provided by the manufacturer in response to an FDA request. The manufacturer responds to FDA's request by submitting an amendment to the original application. Cycle actions on an application can occur repeatedly until FDA determines that the manufacturer has provided what the agency calls a "complete response" to all of the agency's concerns. Then, FDA may make a decision on the application.

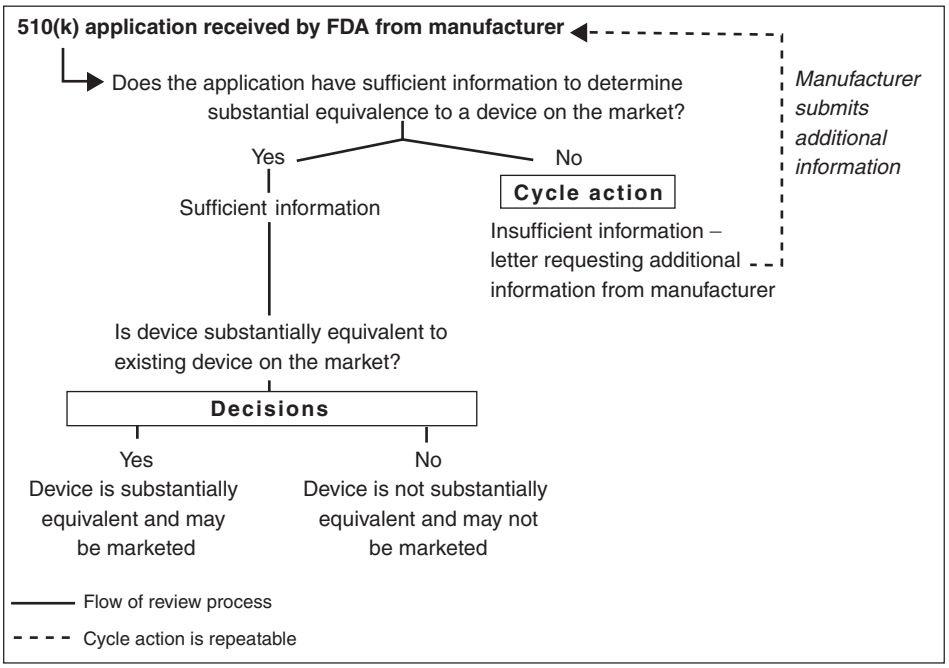
[11]According to FDA, approximately 13 percent of the PMAs, Panel-Track Supplements, and Expedited PMA applications are referred to external advisory committees.

Manufacturers that receive approvable letters pending minor corrections or clarifications or not approvable letters can gain final approval by submitting amendments with complete responses to FDA's concerns. For both types of decisions, if FDA, as part of a cycle action, determines that the manufacturer's amendment is a complete response, FDA issues an order approving the application. If the amendment is not a complete response, FDA issues another approvable letter pending minor corrections or clarifications or a not approvable letter.

The 510(k) Review Process

Under the 510(k) review process, FDA decides whether the application contains sufficient information to determine whether the device is substantially equivalent to one legally on the market (see fig. 2). When a 510(k) application lacks information necessary for FDA to complete its review and make a determination as to whether the device is substantially equivalent, the agency issues a letter requesting additional information from the manufacturer. This request for additional information is a cycle action. The manufacturer may then submit additional information responding to FDA's concerns. Once FDA has obtained complete information from the manufacturer, FDA issues a decision letter informing the manufacturer that the device is substantially equivalent and therefore may be marketed or the device is not substantially equivalent and may not be marketed.

Figure 2: 510(k) Review Process



Source: GAO.

Measuring FDA's Performance under MDUFMA

The MDUFMA performance goals specify a length of time for taking a cycle action, making a decision, or a combination of both. The goals designate a certain percentage of these actions that must occur within the specified period in order for FDA to meet the performance goals. To measure its performance against the MDUFMA performance goals, FDA tracks the time, in calendar days, the agency takes to complete a cycle action or make

a decision—but not the time it takes a manufacturer to respond to a request from FDA.[12]

FDA measures its performance against a specific fiscal year's MDUFMA performance goals using all the applications it received in that year—known as a cohort[13]—regardless of when the final decision is made for each of the applications in that year's cohort. The agency's performance as measured against a fiscal year's MDUFMA performance goals is preliminary until all applications in a cohort are completed—and this can take up to 3 or 4 fiscal years.

The two MDUFMA performance goals that FDA must meet for fiscal years 2003 and 2004 are tied to the same type of cycle action for different types of applications. One performance goal applies to the cycle action taken on PMAs, Panel- Track Supplements, and Premarket Reports, and the other performance goal applies to Expedited PMAs. To meet each performance goal, FDA must review the completeness of a manufacturer's response to an approvable letter pending minor corrections or clarifications and make a decision within 30 days of receiving the manufacturer's amendment. FDA must meet this time frame on 90 percent of the applications for which it takes a cycle action (see table 1).

[12]Except for BLA Resubmissions and BLA Supplement Resubmissions, there are also limits on the length of time manufacturers have to respond to the agency's requests for additional information. For example, as required by FDA regulation, manufacturers submitting amendments to PMAs have 180 days to respond to major deficiency letters. Manufacturers submitting amendments to PMAs can also apply for extensions of up to 180 days beyond the required response time. Manufacturers submitting amendments to 510(k)s have 30 days to respond to first or subsequent letters requesting additional information. For amendments to 510(k)s, manufacturers can apply for extensions of up to 180 days from the date of the first or subsequent letters.

[13]FDA refers to cohorts as "receipt cohorts."

Table 1: MDUFMA Performance Goals for Fiscal Years 2003 and 2004

		Performance goal		
			Percentage of applications received in each fiscal year required to meet review time	
Type of application	FDA cycle actions	Review time	Fiscal year 2003 cohort	Fiscal year 2004 cohort
PMAs, Panel-Track Supplements, and Premarket Reports[a]	Review whether an amendment is a complete response to an approvable letter pending minor corrections or clarifications and make a decision, such as approving the application	30 days	90	90
Expedited PMAs	Review whether an amendment is a complete response to an approvable letter pending minor corrections or clarifications and make a decision, such as approving the application	30 days	90	90

Source: GAO analysis of HHS and FDA information.

[a]FDA groups these types of applications together when measuring performance for this goal.

In fiscal year 2005, 20 MDUFMA performance goals will become effective, including the 2 performance goals that have been effective since fiscal year 2003 (see table 2). The 20 performance goals will apply to eight types of applications identified under MDUFMA and will be tied to other cycle actions and decisions FDA makes on the applications during the review process.

Table 2: MDUFMA Performance Goals for Fiscal Year 2005

		Performance goal	
Type of application	**FDA cycle actions and decisions**	**Review time**	**Percentage of applications received in fiscal year 2005 cohort required to meet review time**
PMAs, Panel-Track Supplements, and Premarket Reports[a]	Cycle action: Issue first major deficiency letter requesting significant information from the manufacturer	150 days	75
	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) as a first action on an application	180 days	75
	Cycle action: Issue second or subsequent major deficiency letter requesting significant information from the manufacturer	120 days	75
	Cycle action: Determine whether an amendment contains a complete response to a major deficiency or not approvable letter	180 days	75
	Cycle action: Review whether an amendment contains a complete response to an approvable letter pending minor corrections or clarifications and make a decision, such as approving the application	30 days	90
Expedited PMAs	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) after taking a cycle action on an application	300 days	70
	Cycle action: Issue first major deficiency letter requesting significant information from the manufacturer	120 days	70
	Decision: Issue decision letter (approval, approvable pending GMP inspection, not approvable, approvable pending minor corrections or clarifications, or denial) as a first action on an application	170 days	70
	Cycle action: Issue a second or subsequent major deficiency letter requesting significant information from the manufacturer	100 days	70
	Cycle action: Determine whether an amendment contains a complete response to a major deficiency or not approvable letter	170 days	70

(Continued From Previous Page)

Type of application	FDA cycle actions and decisions	Performance goal: Review time	Performance goal: Percentage of applications received in fiscal year 2005 cohort required to meet review time
	Cycle action: Review whether an amendment contains a complete response to an approvable letter pending minor corrections or clarifications and make a decision, such as approving the application	30 days	90
180-day PMA Supplements	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) after taking a cycle action on an application	180 days	80
	Decision: Issue a not approvable letter as a first action on an application	120 days	80
	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, or denial) as a first action on an application	180 days	80
	Cycle action: Determine whether an amendment contains a complete response to a not approvable letter	160 days	80
Premarket Notifications (510(k)s)	Decision: Issue decision letter (for example, a letter for a device that may be marketed because it is substantially equivalent to one already on the market, or that may not marketed because it is not substantially equivalent)	90 days	75
	Cycle action: Issue first additional information letter	75 days	70
	Cycle action: Issue second or subsequent additional information letter	60 days	70
BLA Resubmissions and BLA Supplement Resubmissions	Cycle action: Review and act on a Class 1 resubmission to an original BLA or BLA supplement (for example, issue a letter requesting limited labeling or safety information from the manufacturer)	2 months	75
	Cycle action: Review and act on a Class 2 resubmission to an original BLA or BLA supplement (for example, issue a letter requesting data on product safety and effectiveness from the manufacturer)	6 months	75

Source: GAO analysis of HHS and FDA information as of March 31, 2004.

[a]FDA groups these types of applications together when measuring performance for this goal.

Limited Data to Measure FDA's Performance against the MDUFMA Performance Goals

FDA had limited data that could be used to measure the agency's performance against most of the MDUFMA performance goals. Thus, it is uncertain whether FDA will meet the MDUFMA performance goals for fiscal years 2003, 2004, and 2005. For fiscal year 2003, the two performance goals could be applied to 53 applications. However, as of March 31, 2004, only one application was subject to a cycle action tied to one of the two MDUFMA performance goals. In its review of that application, FDA determined that the manufacturer provided a complete response to an approvable letter pending minor corrections or clarifications and made the decision to approve the application within the goal's time frame. For fiscal year 2004, there were no applications subject to the cycle action tied to the two fiscal year 2004 MDUFMA performance goals. In addition, the likelihood of FDA meeting the fiscal year 2005 MDUFMA performance goals is uncertain because FDA had performance data for some, but not all, of the MDUFMA performance goals that will be effective in fiscal year 2005. FDA's performance results could change as the agency completes its actions on all applications for which the performance goals apply.

Limited Data to Measure FDA's Performance against the MDUFMA Performance Goals Established for Fiscal Years 2003 and 2004

Limited data exist to measure FDA's performance against the two MDUFMA performance goals established for fiscal years 2003 and 2004. Our analysis shows that FDA received 43 PMAs, 7 Panel-Track Supplements, and 3 Expedited PMAs in the fiscal year 2003 cohort.[14] As of March 31, 2004, one application—an Expedited PMA—had been subject to the cycle action tied to one of the two MDUFMA performance goals for fiscal year 2003.[15] In its review of this application FDA determined that the manufacturer submitted a complete response to an approvable letter pending minor corrections or clarifications, and approved the application within 30 days. For PMAs and Panel-Track Supplements, the same MDUFMA performance goal applied for fiscal year 2003. However, FDA did not have any applications that required the issuance of an approvable letter. Similarly, none of the 15 PMAs, 1 Panel-Track Supplement, and 8 Expedited PMA applications from the fiscal year 2004 cohort required issuance of approvable letters.

[14]FDA received other types of applications in the fiscal year 2003 and 2004 cohorts, but these types are not connected to the MDUFMA performance goals established for fiscal years 2003 and 2004. FDA did not receive any Premarket Report applications, the fourth type of application tied to the fiscal year 2003 and 2004 MDUFMA performance goals.

[15]The Expedited PMA is tied to one of the two MDUFMA performance goals.

Many of the applications from the fiscal years 2003 and 2004 cohorts were pending within the review process for FDA review actions or manufacturers' responses to FDA. Therefore, FDA's performance results are preliminary. In the fiscal year 2003 cohort, 21 of the 50 PMAs and Panel-Track Supplements and 1 of the 3 Expedited PMAs FDA received were pending as of March 31, 2004. Similarly, in the fiscal year 2004 cohort, 13 of the 15 PMAs, 1 Panel-Track Supplement, and all 8 of the Expedited PMAs FDA received were pending action. Because FDA's performance against the MDUFMA performance goals is based on the percentages of actions the agency takes on applications within required review times, FDA's performance results could change as the agency completes actions on all applications for which the performance goals apply. Data were not readily available from FDA on the status of all pending applications within the review process. FDA anticipates having complete data by the end of fiscal year 2004.

Limited Performance Data to Determine the Likelihood of FDA Meeting the Fiscal Year 2005 MDUFMA Performance Goals

The likelihood of FDA meeting the MDUFMA performance goals for fiscal year 2005 is uncertain because data to measure the agency's performance are limited. Specifically, FDA had data that allowed us to compare its performance against some, but not all, of the 20 MDUFMA performance goals that will be effective in fiscal year 2005. For example, from the fiscal year 2003 cohort, data were available to compare FDA's performance against 17 of the 20 performance goals for fiscal year 2005. FDA took actions on applications tied to 14 of the 17 performance goals within the established goal time frames. For 7 of the 14 performance goals, FDA's performance was based on one or two actions on applications. FDA did not take actions within the established goal time frames on applications tied to 3 of the 17 performance goals. Similarly, from the fiscal year 2004 cohort, FDA had data for 11 of the 20 MDUFMA performance goals. We found that FDA took actions on applications tied to each of the 11 performance goals within the established goal time frames. For 4 of the 11 performance goals, FDA's performance was based on no more than three actions on applications. (See table 3.)

Table 3: Status of FDA's Performance for Fiscal Years 2003 and 2004 Compared to MDUFMA Performance Goals That Become Effective in Fiscal Year 2005

		Performance goal		Percentage of actions taken on applications within goal's established time frame	
Type of application	Cycle actions and decisions	Review time	Percentage of actions required to meet the goal for the fiscal year 2005 cohort	Fiscal year 2003 cohort	Fiscal year 2004 cohort
PMAs, Panel-Track Supplements, and Premarket Reports[a]	Cycle action: Issue first major deficiency letter requesting significant information from the manufacturer	150 days	75	85% (22 of 26 cycle actions)	100% (2 of 2 cycle actions)
	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) as a first action on an application	180 days	75	96% (22 of 23 decisions)	100% (3 of 3 decisions)
	Cycle action: Issue second or subsequent major deficiency letter requesting significant information from the manufacturer	120 days	75	100% (1 of 1 cycle action)	[b]
	Cycle action: Determine whether an amendment contains a complete response to a major deficiency or not approvable letter	180 days	75	89% (8 of 9 cycle actions)	[b]
	Cycle action: Review whether an amendment contains a complete response to an approvable letter pending minor corrections or clarifications and make a decision, such as approving the application	30 days	90	[b]	[b]

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Type of application	Cycle actions and decisions	Performance goal: Review time	Performance goal: Percentage of actions required to meet the goal for the fiscal year 2005 cohort	Percentage of actions taken on applications within goal's established time frame: Fiscal year 2003 cohort	Percentage of actions taken on applications within goal's established time frame: Fiscal year 2004 cohort
Expedited PMAs	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) after taking a cycle action on an application	300 days	70	100% (2 of 2 decisions)	[b]
	Cycle action: Issue first major deficiency letter requesting significant information from the manufacturer	120 days	70	100% (2 of 2 cycle actions)	100% (4 of 4 cycle actions)
	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) as a first action on an application	170 days	70	100% (1 of 1 decision)	100% (1 of 1 decision)
	Cycle action: Issue second or subsequent major deficiency letter requesting additional information from the manufacturer	100 days	70	[b]	[b]
	Cycle action: Determine whether an amendment contains a complete response to a major deficiency or not approvable letter	170 days	70	100% (1 of 1 cycle action)	[b]
	Cycle action: Review whether an amendment contains a complete response to an approvable letter pending minor corrections or clarifications and make a decision, such as approving the application	30 days	90	100% (1 of 1 cycle action)	[b]

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Type of application	Cycle actions and decisions	Performance goal: Review time	Performance goal: Percentage of actions required to meet the goal for the fiscal year 2005 cohort	Percentage of actions taken on applications within goal's established time frame: Fiscal year 2003 cohort	Percentage of actions taken on applications within goal's established time frame: Fiscal year 2004 cohort
180-day PMA Supplements	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, not approvable, or denial) after taking a cycle action on an application	180 days	80	95% (194 of 205 decisions)	100% (15 of 15 decisions)
	Decision: Issue a not approvable letter as a first action on an application	120 days	80	19% (6 of 32 cycle actions)	83% (5 of 6 cycle actions)
	Decision: Issue decision letter (approval, approvable pending GMP inspection, approvable pending minor corrections or clarifications, or denial) as a first action on an application	180 days	80	96% (166 of 173 decisions)	100% (9 of 9 decisions)
	Cycle action: Determine whether an amendment contains a complete response to a not approvable letter	160 days	80	100% (15 of 15 cycle actions)	100% (1 of 1 cycle actions)
510(k)s	Decision: Issue decision letter (for example, a letter for a device that may be marketed because it is substantially equivalent to one already on the market, or that may not be marketed because it is not substantially equivalent)	90 days	75	80% (2,869 of 3,598 decisions)	96% (865 of 904 decisions)
	Cycle action: Issue first additional information letter	75 days	70	58% (1,004 of 1,718 cycle actions)	74% (375 of 504 cycle actions)
	Cycle action: Issue second or subsequent additional information letter	60 days	70	53% (283 of 530 cycle actions)	96% (54 of 56 cycle actions)

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Type of application	Cycle actions and decisions	Performance goal: Review time	Performance goal: Percentage of actions required to meet the goal for the fiscal year 2005 cohort	Percentage of actions taken on applications within goal's established time frame: Fiscal year 2003 cohort	Percentage of actions taken on applications within goal's established time frame: Fiscal year 2004 cohort
BLA Resubmissions and BLA Supplement Resubmissions	Cycle action: Review and act on a Class 1 resubmission to an original BLA or BLA supplement (for example, issue a letter requesting limited labeling or safety information from the manufacturer)	2 months	75	[b]	[b]
	Cycle action: Review and act on a Class 2 resubmission to an original BLA or BLA supplement (for example, issue a letter requesting data on product safety and effectiveness from the manufacturer)	6 months	75	100% (2 of 2 cycle actions)	[b]

Source: GAO analysis of FDA data as of March 31, 2004.

[a]FDA groups these types of applications when measuring performance for this goal. In both the fiscal year 2003 and 2004 cohorts, FDA did not receive any Premarket Report applications.

[b]FDA did not have any applications that required the agency to take the action tied to the performance goal.

As previously mentioned, many of the applications from the fiscal years 2003 and 2004 cohorts are awaiting actions by FDA or responses from manufacturers. Our analysis of the applications pending within the review process shows that of the 4,175 applications received in the fiscal year 2003 cohort, 339, or 8 percent, were pending further action by FDA as of March 31, 2004. Of the 1,781 applications received in the fiscal year 2004 cohort, 859, or 48 percent, were also pending as of March 31, 2004. The number of applications pending varied by application type. (See table 4.) For example, in the fiscal year 2003 cohort, 21—or 42 percent—of the 50 PMAs and Panel-Track Supplements were pending, while 316—or 8 percent—of the 3,914 510(k)s were pending further action by FDA. As FDA completes its actions on more applications, its performance results could change.

Table 4: Applications Pending within FDA's Review Process in the Fiscal Year 2003 Cohort and the First 6 Months of the Fiscal Year 2004 Cohort

	Fiscal year 2003		Fiscal year 2004	
Type of application	Total number of applications	Number (percentage) pending	Total number of applications	Number (percentage) pending
PMA and Panel-Track Supplements		21		13
	50	(42%)	16	(88%)
Expedited PMAs		1		8
	3	(33%)	8	(100%)
180-Day PMA Supplements		1		27
	206	(1%)	42	(64%)
510(k)s		316		810
	3,914	(8%)	1,714	(47%)
BLA Resubmissions and BLA Supplement Resubmissions		0		1
	2	(0%)	1	(100%)
Total		**339**		**859**
	4,175	**(8%)**	**1,781**	**(48%)**

Source: GAO analysis of FDA data.

According to FDA officials, in fiscal year 2003, FDA began implementing activities that are intended to enhance its ability to meet MDUFMA performance goals that become effective in fiscal year 2005. These activities, identified in the Secretary of HHS's November 2002 letter establishing the MDUFMA performance goals, include hiring additional staff, consulting with experts outside the agency more frequently, and holding meetings with manufacturers to ensure high-quality applications are submitted to FDA. For example, in fiscal year 2003, CDRH hired staff for 67 new positions, such as medical officers, scientists, and engineers, to improve the timeliness of its device reviews. As of April 2004, CDRH filled 23 of the 65 positions it plans to fill in fiscal year 2004. CBER also filled each of the 11 full-time equivalent positions that it received in fiscal year 2003 and planned to fill 9 full-time equivalent positions during fiscal year 2004 to improve the timeliness of device reviews as well as other

activities.[16] In addition, to help FDA meet its performance goals, FDA held about 100 meetings with manufacturers to discuss ways to improve the quality of applications prior to their submission.

FDA Obligated over $128 Million for Postmarket Medical Device Compliance Activities and Inspections in Fiscal Year 2002

In fiscal year 2002, FDA obligated about $128 million for postmarket medical device compliance activities, which include inspections of device manufacturers' establishments. FDA obligated about $109 million for compliance activities and about $19 million for inspections. Of the approximately $109 million, FDA obligated about $99 million for postmarket compliance activities that encompass outreach coordination, applied research, and laboratory analyses. Outreach coordination included funds for guidance to field staff on matters such as the reporting of problems with medical devices, epidemiology studies, device recalls, and other activities. Obligations for applied research included funding for activities such as the development of domestic and international standards to help provide reasonable assurance that medical devices are safe and effective. Obligations for laboratory analyses included funding for activities such as FDA laboratory-based investigations and scientific training for FDA inspection staff. FDA also obligated an estimated $10 million in rental expenses for office space for FDA staff who conduct compliance activities.[17]

In fiscal year 2002, of the $19 million obligated for inspections, FDA obligated about $17 million for inspections of domestic and foreign establishments and about $2 million in estimated office space rental expenses for FDA staff who conduct inspections.[18] These inspections included routine surveillance inspections to determine compliance with medical device regulations, inspections resulting from the reporting

[16]CBER did not hire additional staff to work exclusively on device applications because its staff works with both devices and biologics. However, biologics account for the majority of CBER's resources.

[17]FDA does not include rental amounts for each center in its annual budget justification. Rental expenses are reported as a single amount for all centers. Therefore, the amounts obligated for rental expenses are estimated.

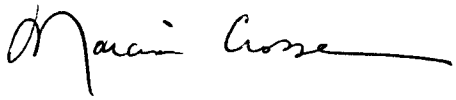
[18]These amounts exclude obligations for inspections of mammography facilities under the Mammography Quality Standards Act of 1992. Mammography inspections are not postmarket device establishment inspections as described in section 704(g)(10)(B) of FDCA.

problems with devices or product recalls, and compliance inspections to collect evidence for pending enforcement actions.

Agency Comments

In commenting on a draft of this report, FDA generally agreed with our findings. FDA stated that it believes the agency has made a good start in its implementation of MDUFMA and FDA believes that its progress in meeting the MDUFMA performance goals is consistent with the extensive performance improvements the agency is expect to achieve each year through 2007. FDA provided technical comments primarily clarifying aspects of the medical device review process, which we incorporated as appropriate. FDA's comments are reprinted in appendix I.

We are sending copies of this report to the Secretary of HHS and the Commissioner of FDA, appropriate congressional committees, and other interested parties. We will also make copies available to others on request. In addition, the report is available at no charge on the GAO Web site at http://www.gao.gov. If you or your staffs have questions about this report, please contact me at (202) 512-7119 or James McClyde at (202) 512-7152. Darryl Joyce, Donna Bulvin, and Krister Friday also made key contributions to this report.



Marcia Crosse
Director, Health Care—Public Health
and Military Health Care Issues

Comments from the Food and Drug Administration

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

August 18, 2004

Marcia G. Crosse, Ph.D.
Director, Health Care – Public Health
and Military Health Care Issues
United States Government Accountability Office
441 G Street, N.W., Room 5A14
Washington, DC 20548

Dear Dr. Crosse:

FDA appreciates the opportunity to review and provide comments on GAO's draft report, *Data to Measure the Timeliness of Reviews of Medical Device Applications Are Limited.* The draft is thorough, provides a good overview of the complex and challenging performance goals FDA is working to achieve under the Medical Device User Fee and Modernization Act of 2002 (MDUFMA), and we generally agree with GAO's findings. We are providing brief technical comments to improve the accuracy and completeness of GAO's description of FDA's medical device review processes and to provide additional suggestions where we believe minor clarifications would be helpful.

I believe FDA has made a good beginning in our implementation of MDUFMA. The performance goals that are the primary focus of your report are a key feature of MDUFMA, but only one of the challenges we are working to meet. We are also working to meet expectations for third-party establishment inspections, the new regulatory requirements for reprocessed single-use devices, and new provisions for pediatric devices. While we work to make these and other improvements, we're also working to ensure that we maintain our performance in areas that don't have specific MDUFMA performance goals.

Although only two of MDUFMA's measurable performance goals were in effect for FY 2003 and FY 2004, our progress to date is, we believe, consistent with the extensive performance improvements we are expected to achieve each year through FY 2007. We will face some significant challenges as we work to meet all of MDUFMA's goals — this is particularly true for MDUFMA's cycle goals — but we believe we are now laying the foundation for future progress, even on the most difficult goals. We are successfully recruiting essential scientific and medical experts and we are expanding our consultation with experts outside the agency; these new resources strengthen our review processes and help us conduct quality reviews in less time. We're working to improve and expand our guidance to industry, to consult with stakeholders as we make policy and program improvements, and to provide additional opportunities for direct communications with applicants. We are mindful of the need to be responsible custodians of the user fees and additional appropriations MDUFMA is providing, and we continue to invest these new resources where they will do the most good for the process for the review of device applications. We're also working hard to modernize our IT infrastructure to enable rapid, efficient reviews, and to position the agency for future electronic submissions and

reviews. We look forward to continued cooperative efforts with all interested parties to ensure the MDUFMA legislation is recognized as an unqualified success.

Along with the entire FDA team, I am strongly committed to meeting MDUFMA's challenging performance goals and to making the other process improvements necessary to provide a fair, transparent, and predictable process to rapidly bring new medical devices to patients and the health care community.

If you have any questions concerning our comments, or need additional information to complete your final report, please feel free to contact me or Linda Kahan, Deputy Director, CDRH. Ms. Kahan may be reached at (301) 827-7975, or by e-mail at linda.kahan@fda.gov. Thank you again for allowing us to review and comment on your report.

Sincerely,

for:
Lester M. Crawford, D.V.M., Ph.D.
Acting Commissioner of Food and Drugs

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