# Memorandum

Date MAR - 6 1996

From Deputy Inspector General
for Audit Services

Subject Review of the Food and Drug Administration's Processes to Review Medical Device Submissions Under the Pre-Market Approval and Investigational Device Exemption Programs (A-15-95-50001)

To David A. Kessler, M.D.
Commissioner of Food and Drugs

The attached final report provides you with the results of our review of the Food and Drug Administration's (FDA) Center for Device and Radiological Health's (CDRH) controls for ensuring the integrity of the Pre-Market Approval (PMA) and Investigational Device Exemption (IDE) application review processes. In March 1992, prompted by concerns regarding alleged improprieties in the review and approval of a particular medical device by FDA's CDRH, Office of Device Evaluation, a Senior Advisor to the Commissioner of Food and Drugs (Senior Advisor) requested that the Office of Inspector General assess the processes and controls for reviewing pre-market applications.

Our overall objective was to examine the status of corrective actions taken in areas reflecting the Senior Advisor's specific concerns about CDRH's processes for reviewing PMA and IDE applications. These areas included: (1) data audits; (2) staff expertise; (3) clinical trial design; (4) review resources; (5) resolution of disputed decisions/ documentation of reviews; and (6) independent quality control reviews.

In general, since 1992, CDRH has taken corrective action that should enhance the integrity of the PMA and IDE pre-market application review processes. However, CDRH could further strengthen the integrity of these decisionmaking processes by fully implementing a program for conducting independent internal quality control reviews. With respect to the areas we reviewed, we found that CDRH took corrective action by: (1) instituting a data audit program in June 1992; (2) increasing the number of scientific experts involved in reviews and expanding training requirements; (3) providing guidance on clinical trial design to industry; (4) implementing procedures for prioritizing resources spent on specific application reviews; and (5) developing a process for resolving disputed decisions and documenting application reviews.

The CDRH implemented a process for conducting independent quality control reviews of IDEs, but not PMAs. We are concerned that CDRH has not fully implemented independent quality control reviews because, over the last several years, serious deficiencies have been determined to exist in the clinical data submitted as part of pre-market applications. When such deficiencies go undetected, medical device approvals may pose health risks for consumers. We believe that an ongoing independent quality

control review program, for PMAs as well as IDEs, would minimize the possibility that device submissions containing clinical data deficiencies become marketed medical devices. We are recommending that CDRH establish a process for conducting independent quality control reviews of the scientific validity of PMA medical device review decisions.

On February 5, 1996, FDA provided its response to our December 1, 1995 draft report. It concurred with our recommendation for CDRH to implement a process for conducting independent quality control reviews of the scientific validity of PMA medical device review decisions, and delineated actions to address our recommendation.

If you have any questions regarding the matters discussed in this report, please call me or have your staff contact Joseph J. Green, Assistant Inspector General for Public Health Service Audits, at (301) 443-3582.

To facilitate identification, please refer to Common Identification Number A-15-95-50001 in all correspondence relating to this report.

Thomas D. Roslewicz

Attachment

Department of Health and Human Services

# OFFICE OF INSPECTOR GENERAL

# REVIEW OF THE FOOD AND DRUG ADMINISTRATION'S PROCESSES TO REVIEW MEDICAL DEVICE SUBMISSIONS UNDER THE PRE-MARKET APPROVAL AND INVESTIGATIONAL DEVICE EXEMPTION PROGRAMS


**JUNE GIBBS BROWN**
**Inspector General**

**MARCH 1996**
**A-15-95-50001**

# Memorandum

Date MAR - 6 1996

From Deputy Inspector General
for Audit Services

Subject Review of the Food and Drug Administration's Processes to Review Medical Device Submissions Under the Pre-Market Approval and Investigational Device Exemption Programs (A-15-95-50001)

To David A. Kessler, M.D.
Commissioner of Food and Drugs

This final report provides you with the results of our review of the Food and Drug Administration's (FDA) Center for Device and Radiological Health's (CDRH) controls for ensuring the integrity of the Pre-Market Approval (PMA) and Investigational Device Exemption (IDE) application review processes.

## OBJECTIVE

Our overall objective was to examine the status of corrective actions taken in areas reflecting the Senior Advisor to the Commissioner of Food and Drugs[1] specific concerns about CDRH's processes for reviewing PMA and IDE applications. These areas included:

(1) data audits;

(2) staff expertise;

(3) clinical trial design;

(4) review resources;

(5) resolution of disputed decisions/documentation of reviews; and

(6) independent quality control reviews.

## SUMMARY OF FINDINGS

In general, since 1992, CDRH has taken corrective action that should enhance the integrity of the PMA and IDE pre-market application review processes. However,

[1] We use the term Senior Advisor when referring to this official.

CDRH could further strengthen the integrity of these decisionmaking processes by fully implementing a program for conducting independent quality control reviews.[2]

With respect to the areas we reviewed, we found that CDRH took corrective action by: (1) instituting a data audit program in June 1992; (2) increasing the number of scientific experts involved in reviews and expanding training requirements; (3) providing guidance on clinical trial design to industry; (4) implementing procedures for prioritizing resources spent on specific application reviews; and (5) developing a process for resolving disputed decisions and documenting application reviews.

The CDRH implemented a process for conducting independent quality control reviews of IDEs, but not PMAs. We are concerned that CDRH has not fully implemented independent quality control reviews because, over the last several years, serious deficiencies have been determined to exist in the clinical data submitted as part of pre-market applications. When such deficiencies go undetected, medical device approvals may pose health risks for consumers. We believe that an ongoing independent quality control review program, for PMAs as well as IDEs, would minimize the possibility that device submissions containing clinical data deficiencies become marketed medical devices.

We are recommending that CDRH:

- establish a process for conducting independent quality control reviews of the scientific validity of PMA medical device review decisions.

On February 5, 1996, FDA provided its response to our December 1, 1995 draft report. It concurred with our recommendation for CDRH to implement a process for conducting independent quality control reviews of the scientific validity of PMA medical device review decisions, and delineated actions to address our recommendation. The FDA provided three technical comments that we addressed where appropriate. Details of the comments and actions are contained in the FDA Comments and the Office of Inspector General (OIG) Response section of this report. In addition, FDA's comments are included in their entirety in Appendix B to this report.

---

[2] The term "independent quality control review" as used in this report refers to a process whereby an independent and technically qualified group of professionals, within CDRH or FDA, periodically reviews randomly selected decisions and makes recommendations for improvement.

## BACKGROUND

Section 515 of the Food, Drug, and Cosmetic Act (the Act) requires a sponsor of a Class III[3] medical device to submit a PMA to be used as the basis for FDA's review process. A PMA review is to determine, on the basis of scientific evidence prepared by the manufacturer, whether the medical device is safe and effective. Section 520(g) of the Act provides manufacturers with an exemption from the requirements of Section 515. This exemption, known as an IDE, is used to encourage the discovery and development of useful medical devices. The IDE permits a medical device to be shipped in interstate commerce for clinical investigation to determine its safety and effectiveness.

In March 1992, prompted by concerns regarding alleged improprieties in the review and approval of a particular medical device by CDRH's Office of Device Evaluation (ODE), a Senior Advisor requested that OIG assess the processes and controls for reviewing pre-market applications. We were specifically requested to assess the review of applications and the adequacy of controls with respect to review policies and training.

The medical device review process became the focus of a number of reviews as a consequence of these allegations. The FDA itself immediately began a series of internal reviews. At the congressional level, the Subcommittee on Oversight and Investigations (Subcommittee), House Committee on Energy and Commerce, critiqued FDA's medical device review process in its May 1993 report entitled, "Less Than The Sum Of Its Parts: Reforms Needed in the Organization, Management, and Resources of the Food and Drug Administration's Center for Devices and Radiological Health (Less Than The Sum of Its Parts)." The integrity of the medical device review process was also the subject of OIG's February 1993 final report entitled, "Follow-up of Internal Control Weaknesses in FDA's Medical Device 510(k) Review Process" (CIN: A-03-92-00605).

## SCOPE

Our overall objective was to examine the status of corrective actions taken in areas reflecting the Senior Advisor's specific concerns about CDRH's processes for reviewing PMA and IDE applications.

To conduct our review, we examined CDRH's PMA and IDE application decisionmaking processes. We also reviewed the status of corrective actions taken in response to FDA and congressional recommendations for enhancing the integrity of CDRH's review procedures.

---

[3] The FDA has placed medical devices into one of three classifications according to the degree of regulation necessary to provide reasonable assurance of their safety and effectiveness. Class I devices are subject to the least regulation and Class III the most.

To conduct our analysis of the PMA and IDE application decision processes, we examined ODE's policies and procedures for conducting these reviews. In addition, we interviewed CDRH officials in management positions to gain an understanding of their views on pre-market device application policies and procedures. We also examined CDRH's implementation of corrective actions by analyzing documentation and interviewing ODE staff members responsible for reviewing pre-market device applications.

During our review, we judgmentally selected 5 PMAs that had been approved by ODE and 7 IDE applications under review to: (1) evaluate CDRH's decisionmaking process itself; (2) determine whether reviewers complied with ODE review policies and procedures; and (3) identify controls for documenting procedures used when analyzing applications.

To determine what corrective actions CDRH took with respect to the PMA and IDE application review processes, we analyzed reports containing recommendations for enhancing the integrity of these processes. These were: (1) FDA internal reports, including the Committee for Clinical Review's 1993 final report; (2) the Subcommittee, House Committee on Energy and Commerce review of its 1993 report entitled, "Less Than The Sum Of Its Parts," and FDA's response to this report; and (3) OIG's February 1993 final report, "Follow-up of Internal Control Weaknesses in FDA's Medical Device 510(k) Review Process." (See Appendix A for more detailed information on these reports.)

Our review was conducted in accordance with generally accepted government auditing standards. Field work was performed at FDA offices in Rockville, Maryland. The scope of our review was limited to reviewing corrective actions taken with respect to the PMA and IDE review processes. We did not assess the adequacy of the actions taken by CDRH.

## DETAILED RESULTS OF REVIEW

In general, CDRH has responded to concerns about the PMA and IDE pre-market application review processes by taking corrective action that should enhance the integrity of these review processes. However, we believe that CDRH should further strengthen the integrity of these decisionmaking processes by implementing an independent quality control review program for PMAs.

In the following paragraphs, we discuss positive actions taken by CDRH to enhance the integrity of its processes for assigning and reviewing PMA and IDE applications. This is followed by a discussion about the need to fully implement a program for conducting independent quality control reviews of PMA and IDE application decisions.

*Significant Action Taken to Enhance Integrity of PMA and IDE Application Review Processes*

During the course of our review, we identified significant actions taken by CDRH including: (1) implementing data audits to ensure the validity of data submitted in support of device applications; (2) bolstering staff expertise to keep pace with medical device technology; (3) expanding clinical trial guidance to strengthen clinical studies submitted by sponsors; (4) emphasizing potential risks and benefits for allocating review resources; and (5) instituting procedures for resolving differences of opinion and documentation of application reviews. These actions, taken in response to the Subcommittee and the Committee for Clinical Review's recommendations, should enhance the integrity of the PMA and IDE pre-market approval decisionmaking processes by strengthening management controls; upgrading the rigor and quality of scientific review; and increasing operational efficiency and predictability.

1. Progress Made in Implementing Data Audit Program

Prior to our review, FDA did not routinely conduct data audits on PMAs and IDEs for the purpose of verifying data included in medical device applications. Since June 1992, however, CDRH has made significant progress implementing an important integrity control--a data audit program for PMAs and IDEs. Currently, data audits are required as a condition of approval for all PMAs. According to FDA, data audits for IDEs are rarely feasible because data is being gathered during the investigation, and is not complete until the study is complete. The IDEs are subject to bioresearch monitoring inspections to ensure investigations comply with relevant regulations, including those aimed at ensuring the integrity of data. If the data submitted as part of an IDE application indicate potential safety problems, a data audit will be performed.

The Office of Compliance's Division of Bioresearch Monitoring[4] (DBM) conducts data audits at the same time that a device application is undergoing review by ODE. Field investigators perform data audits at clinical trial sites by reviewing raw data collected during such trials. Results from this review are then compared with summary data provided to CDRH as part of the application process. According to FDA, ODE reviewers use both raw and summary data in reaching decisions.

---

[4] The DBM is responsible for coordinating and implementing all aspects of the Agency's bioresearch monitoring program for medical devices and radiological health products.

According to DBM officials, 181 routine data audits were conducted on PMA, IDE, and 510(k) applications from June 1992 through May 1995.[5] Improprieties and noncompliance identified during data audits have resulted in DBM's taking 80 enforcement actions, including sending 48 warning letters to device sponsors and rejecting data generated during clinical studies. Sponsors have also voluntarily withdrawn device submissions in seven cases.

2. Staff Expertise Enhanced Through Hiring and Expanding Mandatory Training

During our review, FDA's Committee for Clinical Review and the Subcommittee expressed concern about device reviewers' lack of training and expertise with respect to clinical study design and medical device technology. Beginning in 1993, CDRH responded to these concerns by taking action to enhance staff expertise. Efforts to strengthen staff expertise focused on hiring scientific experts and significantly expanding training requirements.

In 1993, CDRH initiated an aggressive hiring campaign to add clinical expertise to its review staff. By 1994, 135 new employees; including 25 medical officers, 27 scientists, and 42 engineers; had been added to ODE's review staff. In addition, the Committee for Clinical Review's recommendation to better integrate statisticians into the review process has been implemented by increasing the number of such staff and co-locating statisticians[6] and device reviewers within ODE divisions. Responding to the Subcommittee and Committee for Clinical Review's recommendations to expand training, CDRH established a Staff College in 1993 to provide continuing educational opportunities in regulatory science, advancing technology, and regulatory management. The Staff College acted on the Committee for Clinical Review's recommendation to develop specific clinical trial training for reviewers by instituting a mandatory course addressing the issues of clinical design and analysis for all device reviewers.

3. The CDRH Provided Guidance to Industry to Strengthen Clinical Data Submitted As Part of PMA and IDE Applications

In response to the Committee for Clinical Review and the Subcommittee's 1993 report recommendations, CDRH instituted procedures for providing clinical trial guidance to the device industry. By taking such an action, CDRH has clearly articulated its expectations with regard to strengthening the degree of scientific rigor in clinical studies submitted for pre-market review.

---

[5] The DBM officials could not determine the number of data audits that had been conducted for each of these device types. However, the officials stated that PMAs make up the majority of applications for which data audits are performed.

[6] Statisticians report to CDRH's Office of Surveillance and Biometrics.

In September 1993, less than 1 year after the Committee for Clinical Review recommended using workshops as a forum for discussion of sound clinical design concepts, CDRH organized its first such workshop for device industry officials. Acting on the Committee's recommendation to develop guidance on the design and analysis of studies, as well as the format and content of submissions for specific device classes, each CDRH division issued guidance documents for specific devices. According to ODE officials, 48 of these guidance documents were issued by all divisions in 1994. The CDRH is currently in the process of obtaining comments and finalizing a number of overall guidance documents addressing various aspects of clinical design.

In July 1995, CDRH issued guidance formalizing innovative procedures designed to strengthen clinical data submitted in support of IDE applications. This guidance includes procedures encouraging sponsors to begin communicating with a reviewing division, in the form of a pre-IDE meeting and/or a pre-IDE submission, before an application is submitted for formal review. Pre-IDE meetings are intended to facilitate the initiation of clinical trials which conform to IDE regulations. In addition, sponsors are encouraged to prepare pre-IDE submissions so that ODE staff can provide informal guidance for areas such as clinical protocol design and pre-clinical testing before a formal application is submitted.

Taking the Committee for Clinical Review's findings into account, CDRH also expanded its use of advisory committees to include holding closed panel sessions to provide feedback on clinical designs proposed for IDE submissions. In addition, the Clinical Trials Board, a pilot program established in 1994 as part of ODE's Division of Cardiovascular, Respiratory, and Neurological Devices, serves as a forum for evaluating IDE submissions to the division to determine the appropriateness of clinical design and necessary modifications.

4. Procedures Implemented for Prioritizing Review Resources

During our current review, CDRH responded to the Subcommittee's call to develop procedures for prioritizing review resources on the basis of a device's potential health benefit and level of risk, and on the sufficiency of a device application's completeness for review. Such policies include the following:

-- Expedited review - provides a separate, expedited approval track for medical devices possessing unique public health benefits.

-- Triage - enables applications to be assigned for review based on the inherent risk of the device itself. According to ODE, this procedure allows for an appropriate level of effort to be expended since device submissions vary in their complexity and risk.

-- Refuse-to-file - specifies criteria for determining if a PMA device application is sufficiently complete to be accepted for review.

-- Refuse-to-accept - specifies criteria for determining if an IDE device application is sufficiently complete to be accepted for review.

-- The 510(k) Exemption Program - exempts certain types of Class I devices from being subject to the 510(k) pre-market notification process. According to ODE, this program, which has exempted approximately 160 types of devices since 1994, and proposed exemptions for an additional 124 types of devices, allows reviewer resources to be more effectively applied to other more important applications.

The CDRH views these policies as an attempt to ensure that it applies scarce resources to the most important, complete device applications. Such policies, if fairly and fully implemented, could contribute significantly to enhancing the integrity of the PMA and IDE application review processes.

5. Process Developed for Resolving Disputed Decisions and Documenting Reviews

The CDRH finalized procedures for resolving disputed decisions and documenting application reviews in December 1993. This action followed the Subcommittee's recommendation to overcome organizational deficiencies hindering CDRH's performance by, among other things, developing a process to resolve disputed reviewer decisions.

In December 1993, CDRH finalized guidance describing the respective roles of staff and other persons who may provide input on review documents. The guidance provides review staff with a description of how each person in the review chain is to document their views and the procedure for resolution of differences of opinion should these arise. This guidance should strengthen reviewers' controls for documenting disagreements and discussion which may arise during the PMA and IDE application review processes.

*Independent Quality Control Reviews Have Not Been Fully Implemented*

Our assessment of corrective actions taken to enhance the integrity of the PMA and IDE pre-market approval processes revealed that CDRH has not fully implemented a process for conducting independent quality control reviews. An independent quality control review program has been fully implemented for IDEs. However, such a program does not exist for the PMA application process. Instituting a process for conducting such reviews, as it has for IDEs, would allow CDRH to independently evaluate the scientific decisionmaking used as the basis for PMA application reviews. Such quality control reviews are distinct from the corrective actions we described previously because they provide an overall check on internal controls to assure the quality of medical device products regulated by CDRH. The CDRH could implement independent quality control

reviews for PMAs by independently selecting a random sample of completed PMA decisions for quality control reviews.

We are concerned that CDRH has not fully implemented this important recommendation because, over the last several years, serious deficiencies have been determined to exist in the clinical data submitted as part of pre-market applications. When such deficiencies go undetected, medical device approvals may pose health risks for consumers.

Subcommittee Recommended a Quality Assurance Function

In its May 1993 report, the Subcommittee recommended that within 6 months to 1 year, CDRH develop and implement a sound quality assurance program.[7] It specifically recommended that CDRH establish an independent and technically qualified group of professionals to periodically review approval decisions, and to make recommendations for management or reviewer performance improvements.

In making this recommendation, the Subcommittee noted that FDA's Committee for Clinical Review had uncovered serious scientific deficiencies in the clinical data submitted in support of pre-market device applications. Such deficiencies included inadequate sample sizes; failure to define study endpoints; and failure to use the most appropriate controls.

According to the Committee for Clinical Review, these and other scientific deficiencies were "sufficiently serious to impede the agency's ability to make the necessary judgments about the safety and effectiveness" of the devices under review. The Subcommittee believed--and we tend to agree--that an ongoing independent quality control review program would have exposed the deficiencies prior to the formation of the Committee for Clinical Review. Ongoing retroactive reviews would allow the agency to monitor the quality of data submitted as part of medical device submissions as well as identify areas in need of further improvement.

Need Continues for Independent Quality Control Reviews

In response to the Committee's 1993 report findings, CDRH's Director initiated a follow-up effort--the Tier 2 review--to determine if past deficiencies in clinical design and data analysis continue to undermine the clinical performance of marketed devices. Similar to the review performed by the Committee for Clinical Review, the Tier 2 review identified deficiencies in clinical trial data used as the basis for approval of specific devices. For example, Tier 2 reviewers found a lack of sufficient clinical follow-up data on patients treated with a critical device, while a reviewer questioned the integrity and methodology in parts of the statistical analysis provided in support of another device. Even after

---

[7] We use the term independent quality control review throughout this report.

learning that these and other problems continued to be evident for such devices, CDRH did not take action to implement a formal independent quality control review for PMAs.

Below, we describe the current quality review processes for IDEs and PMAs, and why we believe the need continues for independent quality control reviews.

IDEs

In 1994, CDRH began taking action to implement a quality control review program for IDEs. According to ODE officials, completed IDE decisions are randomly selected for such quality control reviews. The ODE officials who make these selections also conduct the quality control reviews. These officials are not involved in IDE application reviews.

PMAs

Cognizant CDRH officials informed us that PMAs undergo two forms of quality control reviews--one through the advisory panels and another through ODE's application review and supervisory processes. We concluded, however, that these controls do not constitute the type of independent quality control review program recommended by the Subcommittee. Although the advisory panels review all PMA applications as part of the medical device review process, its recommendations are only advisory in nature. As for the ODE review process, we recognize its value as a process to ensure that device reviewers carry out administrative procedures when reviewing PMA applications. We also recognize that FDA has taken steps to use designated experts as part of the ODE review process. However, ODE's review procedures do not provide for independent, retrospective reviews of the scientific validity of application decisions.

An Independent Quality Control Review Program for PMAs Would Benefit CDRH

While we understand that establishing an independent quality control review program for PMAs would have resource implications for CDRH, we believe the benefits that could accrue to the medical device review program would be substantial, and could ultimately help prevent unsafe or ineffective critical devices from endangering the public. For the program to be most effective, the independent quality control reviewers should have access to all the data and reports used by the original PMA reviewers, and be able to recommend to CDRH's management the reversal of PMA decisions.

Given the potential health risks posed by devices reviewed under the PMA review process, and the fact that FDA has revealed previous problems with certain submissions, we reiterate the Subcommittee's recommendation to develop and implement an independent quality control review program.

## RECOMMENDATIONS

We recommend that CDRH:

- establish a process for conducting independent quality control reviews of the scientific validity of PMA medical device review decisions.

## FDA COMMENTS AND OIG RESPONSE

In its February 5, 1996 response to our December 1, 1995 draft report, FDA stated that it fully concurred with our recommendation and indicated that it is implementing independent quality control reviews for PMAs. The FDA is forming a Quality Review Program Committee consisting of three members: one from the ODE (from a division different than the one that performed the original review); one from another CDRH office; and one drawn from the medical device advisory committee members or consultants. According to FDA, the Quality Review Program Committee members are to have the experience, technical knowledge, and independence necessary to conduct meaningful reviews of PMA decisions. The FDA plans to review one PMA each quarter, randomly selected from recent approvals. The results of each review are to be provided to all ODE divisions.

We believe FDA's actions, if fully implemented, should provide the agency with a valuable mechanism for detecting problems in PMA reviews and for bolstering the quality of the overall PMA process.

The FDA provided three technical comments that we addressed where appropriate.

---

To facilitate identification, please refer to Common Identification Number A-15-95-50001 in all correspondence relating to this report.

Thomas D. Roslewicz

# APPENDICES

This appendix contains a detailed description of the reports cited in the Scope section of this report.

(1) FDA internal reviews:

(A) Committee for Clinical Review: At the request of the Commissioner of Food and Drugs, the Committee was formed in April 1992 to provide clinical support to CDRH. The Committee, composed of 12 experienced reviewers from the Center for Drug Evaluation and Research, performed clinical reviews of 29 PMAs, IDEs, and 510(k) device applications pending or recently approved by CDRH. In its March 1993 report, the Committee recommended specific corrective actions for improving the quality of device submissions and enhancing the review process.

(B) Tier 2 Review: In March 1993, upon issuance of the Committee for Clinical Review's report, the Director of CDRH formed a committee of clinical experts from CDRH's ODE to conduct a second, retrospective review of devices approved by CDRH. The purpose of this review was to determine if clinical study design deficiencies identified by the Committee for Clinical Review undermined the clinical performance of marketed devices. The Tier 2 committee reviewed 24 510(k) and PMA devices that had been submitted for review beginning in 1988. The Tier 2 review was never finalized or released to CDRH staff for review.

© Management Action Plan (MAP): In September 1992, CDRH issued a MAP outlining actions for strengthening the device review process and post-market management of its programs. A final MAP was issued in September 1993.

(2) Congressional Review and FDA Response:

(A) Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce review: the Subcommittee conducted a review of the medical device process and issued a May 1993 report entitled, "Less Than The Sum Of Its Parts." This report contained a number of recommendations for corrective action in the medical device approval process. Specific corrective actions included: (1) short-term actions to increase scientific rigor; (2) intermediate actions to implement quality assurance as part of reviewer training and resolve internal disputes in an accountable manner; and (3) long-term actions creating a credible internal review capability as well as increased technical and scientific expertise to support device regulation.

(B) FDA Response: In September 1993, FDA provided the Subcommittee with a written response providing an overview of the policy and procedural reforms already underway in the medical device program.

(3) OIG Review:

(A) 510(k) Follow-up Review: Our 510(k) follow-up review examined ODE's policies and procedures for processing pre-market medical device applications. Our February 1993 report recommendations for enhancing internal controls in the medical device review process included initiating independent quality control reviews of medical device application decisions, and conducting audits of scientific data that sponsors submit to support such applications.

## OTHER IG REPORTS

Investigational Devices: Four Case Studies, April 1995, OEI-05-94-00100

-- This review, requested by FDA, used a case study methodology to assess whether controls over clinical testing of investigational devices ensure patient safety and sound clinical research. The OEI reported that its findings raised serious concerns about the efficacy and reliability of the current oversight process.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

# Memorandum

Date FEB - 5 1996

From Deputy Commissioner for Management and Systems (Acting)

Subject Food and Drug Administration's (FDA) Comments on the Office of Inspector General's (OIG) Draft Report, "Review of the FDA's Processes to Review Medical Device Submissions Under the Pre-Market Approval and Investigational Device Exemption Programs," (A-15-95-50001) - INFORMATION

To Acting Deputy Inspector General for Audit Services

We reviewed the referenced draft report and prepared the attached comments.

The FDA's Center for Devices and Radiological Health has agreed with your report's recommendation and is beginning to implement it.

If your staff has any questions, please have them contact Jim Dillon on (301) 443-6392.

Robert J. Byrd

Attachment

# COMMENTS OF THE FOOD AND DRUG ADMINISTRATION ON THE OFFICE OF INSPECTOR GENERAL (OIG) DRAFT REPORT, "REVIEW OF THE FDA's PROCESSES TO REVIEW MEDICAL DEVICE SUBMISSIONS UNDER THE PRE-MARKET APPROVAL AND INVESTIGATIONAL DEVICE EXEMPTION PROGRAMS," A-15-95-50001 DECEMBER 1, 1995

## General Comments

We appreciate the opportunity to review and comment on the referenced OIG draft report.

The Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) is pleased that the OIG, as reflected in their report, recognizes the significant progress the Center has made in improving FDA's pre-market approval (PMA) and investigational device exemption (IDE) programs over the past few years. CDRH commends the OIG's study team for all of their efforts, especially for assimilating a vast amount of data in a relatively short period.

## OIG Recommendation

We recommend that CDRH establish a process for conducting independent quality control reviews of the scientific validity of PMA medical device review decisions.

### FDA Comment

FDA concurs. CDRH is implementing a quality review program for PMAs that will use review committees consisting of three members: one from CDRH's Office of Device Evaluation (ODE), one from another CDRH office, and one drawn from the Medical Device advisory committee members or consultants. The representative from ODE will not be from the division that performed the original review.

The Quality Review Program Committee members will have the experience, technical knowledge, and independence necessary to conduct meaningful quality control reviews of PMA decisions. One PMA will be reviewed each quarter, randomly selected from recent approvals. The results of each review will be provided to all ODE divisions.

Technical Comments

Pages 1, 2, 3, 8, 9 and 10

The term, "independent quality control review," as used in the report, is not explained until page 8. To improve the clarity of the report, we recommend that the term be defined the first time it is used in the body of the report. We suggest that definition adequately explained the word, "independent," to show whether it means within the Agency or within CDRH.

The OIG may wish to consider providing additional explanation to address whether the reviewers would deal with all of the data or only with the reports, and whether they can reverse decisions.

Page 5, first paragraph, first line (under previous page's section on "Progress Made in Implementing Data Audit Program")

The statement that "very few IDEs are subject to data audits" is somewhat misleading. Data audits are rarely feasible with IDEs, because data is being gathered during the investigation, and is not complete until the study is complete. IDEs are subject to comprehensive bioresearch monitoring inspections to ensure investigations comply with FDA's IDE regulations; these regulations include provisions that help ensure the integrity and reliability of data developed during the investigation.

Page 5, second paragraph, fourth sentence

The statement that "ODE medical device reviewers perform analysis of summary data only" is not entirely accurate. PMA reviewers receive the same data as reviewers in the Division of Bioresearch Monitoring and may use both summary and raw data in reaching a decision.