

M E M O R A N D U M

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

Date: November 27, 2001
To: Dockets Management Branch (HFA-305)
From: Melissa Lamb
Office of Generic Drugs
Subject: Update from the Office of Generic Drugs

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: Update from the Office of Generic Drugs
Presented for: Generic Pharmaceutical Association
Date Presented: April 10, 2002
Presented by: Gary J. Buehler, R.Ph.,
Director, Office of Generic Drugs
Number of Pages: 18



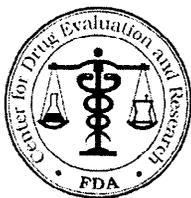
Attachment

90S-0308

M 726

Generic Pharmaceutical Association

2002 Annual Meeting and Educational Conference



Update from the Office of Generic Drugs

Gary J. Buehler

Director

April 10, 2002

Topics

- Office Productivity - Review of Actions
- 2002 Appropriations
- Goals and Objectives
- 2003 Appropriations
- Electronic Submissions Update
- CMC Issues

Office Productivity

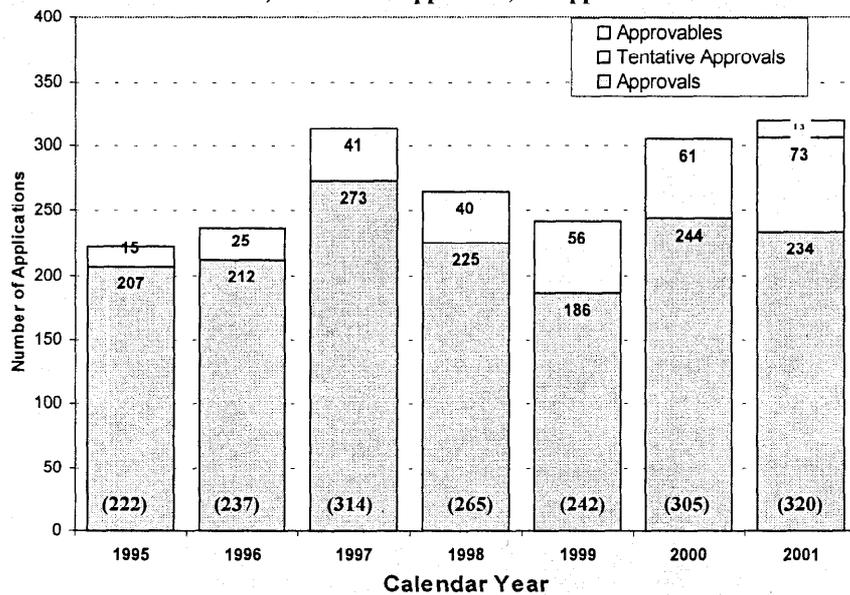
■ Receive, Review and Approve...



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Generic Drug Approvals: Full, Tentative Approvals, & Approvables

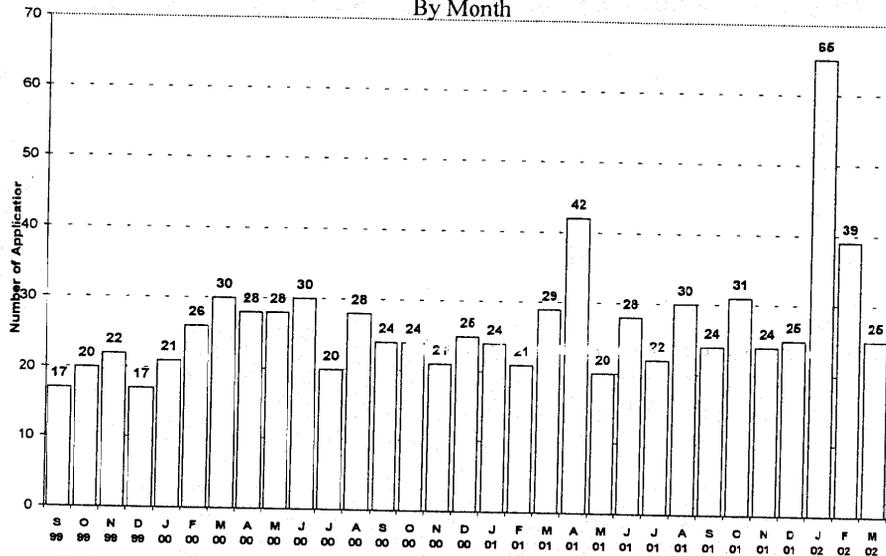


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Generic Drug Approvals: Full, Tentative Approvals, & Approvables

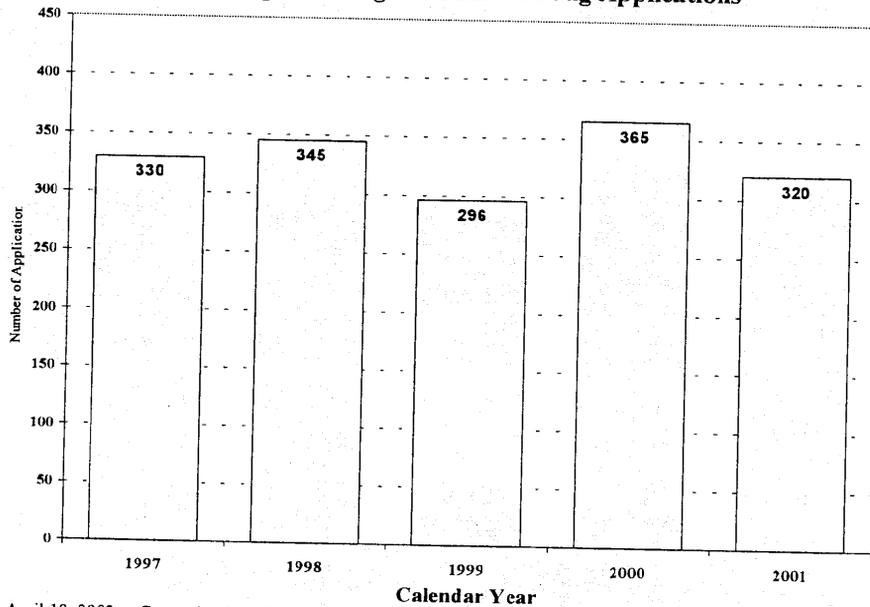
By Month



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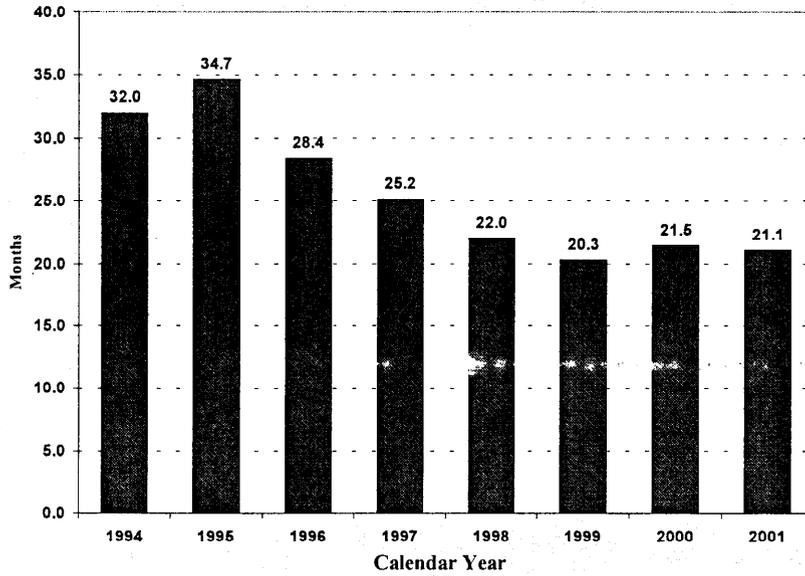
Receipts of Original Generic Drug Applications



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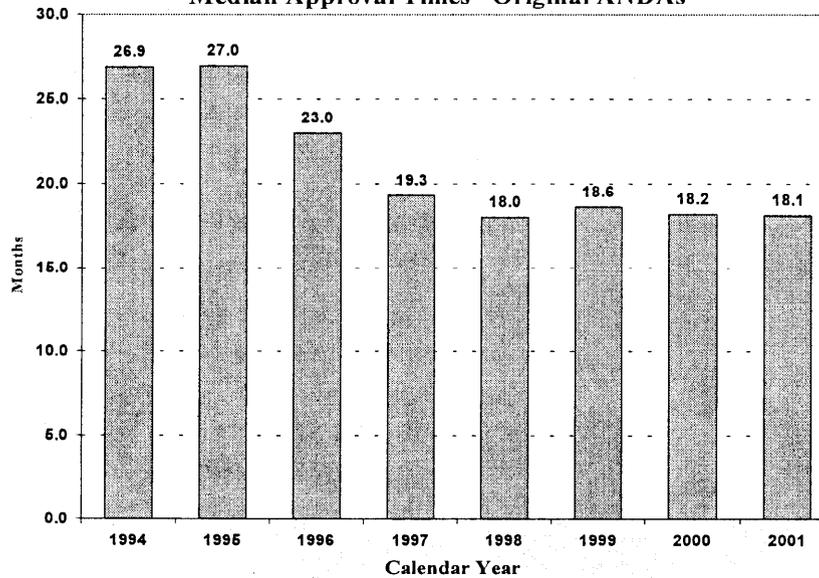
Office of Generic Drugs
Mean Approval Times - Original ANDAs



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Office of Generic Drugs
Median Approval Times - Original ANDAs



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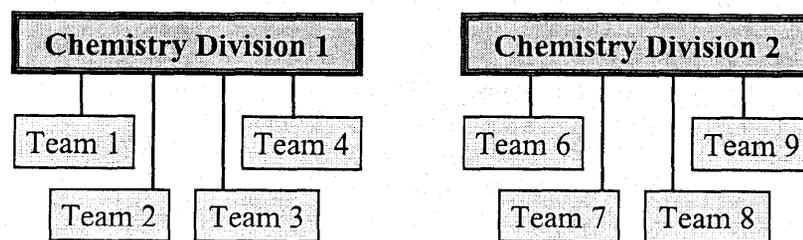
FY 2002 Appropriations

■ Targets:

- ❖ Increased Staffing
- ❖ Dollars for Public Awareness Campaign

Chemistry Staffing

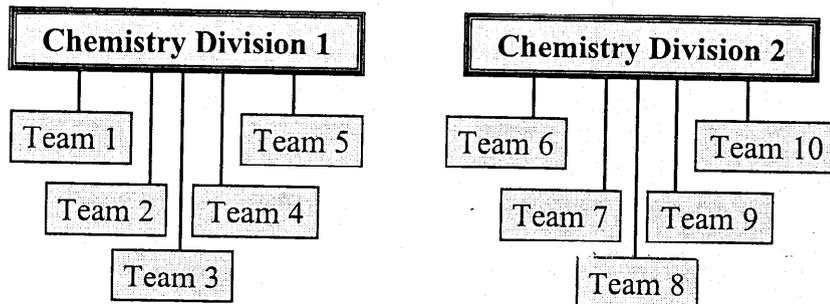
Current organization



■ 2 Divisions with 4 Teams Each

Chemistry Staffing

Proposed organization by FY 2002



- 2 Divisions with 5 Teams Each

Goals

- Decrease total time to approval
- Increase OGD science base
- Hiring and retention
- Generic drug quality awareness program
- Timely foreign inspections
- Fully address legal issues

Decrease Time to Approval

- Modify designation of major and minor amendments
- Hiring additional review chemists
- Exploring numerous “efficiencies”
 - ❖ Additional staff for tertiary and first generic reviews
- Re-alignment of Chemistry Teams
- Cooperation from Industry

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Increase Science Base

- Acting Deputy
 - ❖ Policy development
 - ❖ Scientific strength
- Expand scientific capability of OGD reviewers
- Foster scientific exchange among regulatory, industrial, and academic scientists
 - ❖ Work with OGD Education Committee
- Further integrate scientific knowledge and experience into generic drug approval process

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Increase Science Base

(continued)

- Oversight on all citizen petition responses and correspondence challenging generic approvals
- Internal scientific seminar on polymorphism
- Identification of scientific research projects for the Office of Testing & Research (OTR)
 - ❖ Could include major research initiatives into alternate bioequivalence methods

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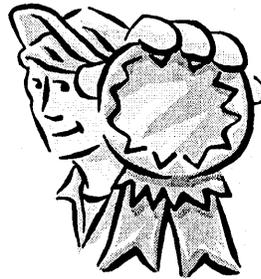
Hiring and Retention

- Portion of appropriation for staff training
- 14 new full-time positions
- Focus on retention of staff
 - ❖ Scientific seminars
 - ❖ Updated equipment
 - ❖ Professional development
 - ❖ Retreats with staff to solicit feedback
- Enriched scientific exchange

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Generic Drug Quality Awareness Program



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Timely Foreign Inspections

- Could be rate limiting step if total time to approval is decreased
- Additional compliance staff funded
- Critical to assure generic drug quality

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Fully Address Legal Issues

- Additional Office of Chief Counsel (OCC) staff
- Actions well grounded in the statute and regulations
- Cooperate with OCC to improve communication with respect to legal issues

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Section 505(j)(2)(A)(viii)

“Little or Section 8 statement”

- For method of use patents
- Cannot be used to circumvent paragraph IV certification process or for settling disputes over patent protection

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Section 505(j)(2)(A)(viii)

(continued)

- Appropriate only when generic drug labeling is carved out to avoid infringement of a listed method of use patent
- A paragraph IV certification is the proper method to challenge a listed patent.

OGD Procedures

- Applicants should specify in their applications what part of the approved labeling will be deleted when using the “little viii” statement.
- If this is not done, you should receive a call from the Regulatory Support Team prior to filing.

FY 2003 Appropriations

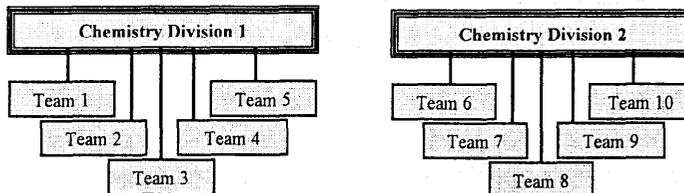
- Additional funding for FY03 has been proposed in the President's budget
- \$4.582 million has been proposed with the following general breakdown:
 - ❖ \$1.146 million to ORA field activities to address inspection capabilities
 - ❖ \$3.346 million to OGD and support offices
- Continue to address review efficiency

FY2003 Appropriations

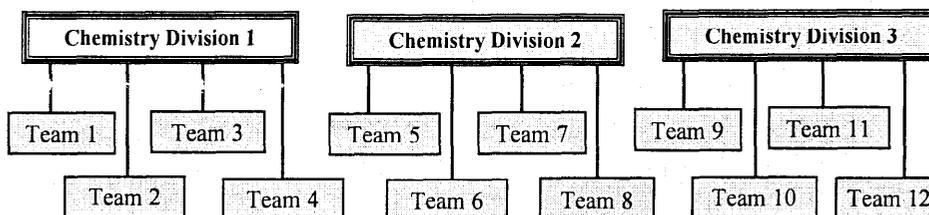
(continued)

- Continue to expand our science base
- Continue to support other areas in CDER and the Agency -
 - Office of Chief Counsel
 - Office of Pharmaceutical Science
 - Office of Compliance
 - Division of Scientific Investigations

From FY2002 Organization



Proposed FY2003 Organization

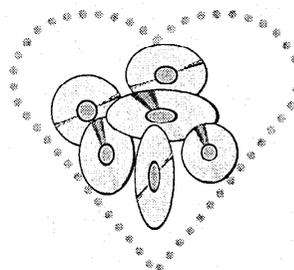
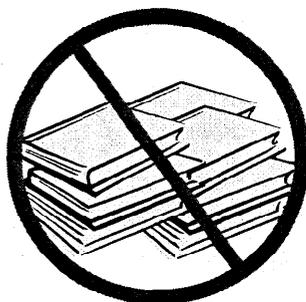


■ 3 Divisions with 4 Teams Each

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A Word on Electronic Submissions



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Providing Regulatory Submission in Electronic Format --ANDAs

- Draft guidance published November 2001
- Comment period closed January 2002
 - ❖ Comments (2):
 - Consistency with CTD format (and e-CTD) format
- Final Guidance very close to publication
- Provides for consistency with current NDA format, change to CTD format and eventual e-CTD format

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More Information

www.fda.gov/cder/regulatory/ersr/default.htm

www.fda.gov/cder/m2/eCTD.htm

Ruth Warzala, OGD 301-827-5845

ERSR Technical Support esub@cder.fda.gov

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CMC Issues - Stability

■ Stability Guidance

- ❖ at the review stage
- ❖ priority lowered because of CDER commitment to implementation of the ICH CTD
- ❖ CDER Drug Substance and Drug Product Guidances are critical to CTD implementation to they have assumed a higher priority than the Stability Guidance

CMC Issues - Stability

■ ICH-Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Drug Products

- ❖ Reached Step 4 (Feb 2002, accepted by ICH)
- ❖ Addressed principles in determining suitability of bracketing and matrixing programs
- ❖ Describes sample protocols
- ❖ Although an extension of Q1AR, it is not intended to exclude ANDAs

CMC Issues - Stability

Bracketing and Matrixing (continued)

■ OGD Current practice

- ❖ Package bracketing is standard
- ❖ Matrixing is rare for original applications and treated case by case post-approval
- ❖ Can be proposed in correspondence

CMC Issues - Impurities

■ New Q3AR document - (Drug Substance)

- ❖ Qualification Threshold no longer the same as Identification Threshold

- ID Threshold = 0.10%

- Qual Threshold = 0.15%

- ❖ Reporting is two decimal places - rounding is described
- ❖ We plan to revise OGD Impurities in Drug Substance Guidance accordingly

■ Q3BR (Drug Product) on hold until Q3AR finalized

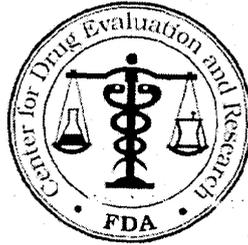
CMC Issues - API Suppliers

- Critical to application
- Supporting DMFs must be reviewed
- Manufacturing sites must be inspected
- Choose carefully

Final Words...

- Proud of what the Generic Drug Industry has accomplished
- Proud of my Office's contribution
- Pleased the Generic Industry speaks with one voice
- GET INVOLVED - Contribute Expertise
 - ❖ Legal Issues
 - ❖ Scientific Issues

Office of Generic Drugs



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SUPPORTING STATEMENT FOR REPORTS OF CORRECTIONS AND REMOVALS

21 CFR PART 806

A. JUSTIFICATION

1. Circumstances Necessitating Information Collection

The Food and Drug Administration (FDA) is amending its regulation in 21 CFR Part 806 Medical Devices; Reports of Corrections and Removals (Attachment A), to eliminate the requirement for distributors to submit reports to FDA. The amendments are being made to implement section 519(f) (21 U.S.C. 360i(f)) of the Federal Food, Drug, and Comestic Act (the act) (21 U.S.C. 301), as amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105-115) (Attachment B).

The information collection requirements in part 806 prior to this direct final rule have been approved by OMB and assigned control number 0910-0359. When preparing the earlier package for approval of the information collection requirements in part 806, FDA reviewed the reports of corrections and removals submitted in the previous 3 years under 21 CFR part 7 (the agency's recall provisions). During that period of time, no reports of corrections or removals were submitted by distributors. For that reason, FDA did not include distributors among the respondents estimated in the collection burden for the requirements previously approved by OMB. Because distributors were not included in that earlier estimate and because FDAMA now has eliminated requirements for distributor reporting, FDA has determined that estimates of the reporting burden Secs. 806.10 and 806.20 should remain the same.

The FDA is requesting approval from the Office of Management and Budget (OMB) for the collection of information required by the amendments to 21 CFR Part 806 promulgated under the statutory mandate of section 519(f) of the act as amended by FDAMA. Below is a description of the information collection requirements in 21 CFR Part 806:

21 CFR 806.10 - Reporting - Each device manufacturer or importer shall submit a written report to FDA of any action initiated to correct or remove a device to reduce a risk to health posed by the device or to remedy a violation of the act caused by the device which may present a risk to health within 10-working days of initiating such correction or removal.

21 CFR 806.20(a) - Recordkeeping - Each device manufacturers or importer of a device who initiates a correction or removal of a device that is not required to be reported to FDA, shall keep a record of such correction or removal.

2. How, By Whom, and For What Purpose Information Is Used

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SSI

The information collected in the reports of corrections and removals will be used by FDA to identify marketed devices that have serious problems and to ensure that dangerous and defective devices are removed from the market. This will assure that FDA has current and complete information regarding these corrections and removals and to determine whether recall action is adequate. Failure to collect this information prevents FDA from receiving timely information about devices that may have a serious effect on the health of the users of the devices.

3. Consideration of Information Technology

In the **Federal Register** of March 20, 1997 (62 FR 13430) (Attachment C), FDA published a final rule establishing procedures for electronic records, electronic signatures, and electronic submissions. Manufacturers or importers may use appropriate technology in accordance with this rule to comply with the reports of corrections and removals requirements.

4. Identification of Duplication and Similar Information Already Available

FDA is the only federal agency responsible for the collection of this information. No data exist from any other source that can be used to report corrections and removals subject to this direct final regulation.

5. Small Businesses

The information collection will not have a significant impact on a substantial number of small entities. FDA's Division of Small Manufacturers Assistance (DSMA) and small business representatives in its six regional offices, aid small businesses subject to medical device regulations. FDA's scientific and administrative staff also provide assistance upon request or through public meetings.

6. Consequences of Less Frequent Information Collection

FDA does not require a specific frequency for this collection. Written reports are to be submitted to FDA only if a manufacturer or importer of a device undertakes a corrective or removal action to reduce a risk to health posed by the device or to remedy a violation of the act.

7. Inconsistencies with 5 CFR 1320.6

This information collection is consistent with 5 CFR 1320.6.

8. Consultations Outside FDA

In the **Federal Register** of August 7, 1998 (63 FR 42229), FDA published a direct Final Rule. (Attachment C). There were no comments received.

9. Payments or Gifts to Respondents

No payment or gifts in any manner or from shall be provided to respondents under this final regulation.

10. Confidentiality of Information

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. Reports and other information submitted to FDA under 21 CFR Part 806 are releasable if they fall within the scope of the agency's regulation concerning "Public Information" (21 CFR Part 20) (Attachment K). However, FOIA exempts disclosures of certain government records from mandatory public disclosures (5 U.S.C. 522(b)(1-9)). One such provision exempts from public disclosure "trade secrets" and "confidential commercial or financial information" that is privileged (5 U.S.C. 522(b)(4)).

11. Sensitive Questions

This information collection does not include questions pertaining to sexual behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature.

12. Burden and Cost to Respondents

Based on previous experience, FDA estimates a total annual cost of \$396,000 to comply with this regulation; \$264,000 to prepare and assemble written reports required by 21 CFR 806.10, and \$132,000 to maintain records of corrections and removals required by 21 CFR 806.20 that will not have to be reported to the agency.

FDA estimates the burden of this collection of information as follows:

Table 1--Estimated Annual Reporting Burden¹

| 21 CFR Section | No. of Respondents | Annual Frequency per Response | Total Annual Responses | Hours per Response | Total Hours |
|----------------|--------------------|-------------------------------|------------------------|--------------------|-------------|
| 806.10 | 88 | 1 | 880 | 10 | 8,800 |

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 2--Estimated Annual Recordkeeping Burden¹

| 21 CFR Section | No. of Recordkeepers | Annual Frequency of Recordkeeping | Total Annual Records | Hours per Recordkeeper | Total Hours |
|----------------|----------------------|-----------------------------------|----------------------|------------------------|-------------|
| 806.20 | 440 | 1 | 440 | 10 | 4,400 |

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

21 CFR 806.10 Reporting

FDA estimates that it would take 10 staff hours to prepare and assemble a written report. At an average of \$30 per staff-hour, the cost to prepare and assemble a report is \$300 (10 staff-hours x \$30 per staff-hour). For the estimated 880 reports, the final total cost would be \$264,000 (880 reports x 300 per report).

21 CFR 806.20 Recordkeeping

FDA estimates that it would take 10 staff-hours to prepare a written record at an average cost of \$30 per staff hour. For the estimated 440 records, the total cost would be \$132,000 (440 records x 300 per record).

13. Estimated Annual Cost to Respondents or Recordkeepers

There are no additional annual cost burdens associated with the collection of information beyond what is identified in the annualized hourly reporting and recordkeeping burden. No additional capital expenditures or related service expenses are required or associated with the reporting or recordkeeping requirements other than customary and usual business practices or required to achieve regulatory compliance with other FDA regulatory requirements.

14. Estimated Annual Cost to Government

FDA estimates that the Federal government will use 1 FTE's to implement the Reports of Corrections and Removals regulations required by section 519(f) of the act. Based on a cost of \$55,969 (the agency's average cost of an FTE, including benefits) per position at the GS-13 grade level, the estimated annual cost is \$6155,659.

| <u>FTE</u> | <u>Cost Per FTE</u> | <u>Total Cost</u> |
|------------|---------------------|-------------------|
| 11 | \$52,867 | \$581,537 |

15. Changes in Burden

There are no changes in the estimated reporting and recordkeeping burdens.

16. Publication of Results

No tabulation of the data is planned or anticipated.

17. Exemption for Display of Effective Date

FDA is not seeking approval to prevent the display of expiration date or OMB approval of this request.

18. Exception to Certification Statement

There are no exceptions to the certification statement identified in item 19 of OMB Form, 83 - I.

B. Collection of Information Using Statistical Methods

The use of statistical methods is not applicable because all removals and corrections of medical

devices are subject to the reporting or recordkeeping requirements.