Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

FDA's Review Process for New Drug Applications

A Management Review

JANET REHNQUIST
INSPECTOR GENERAL

MARCH 2003

OFFICE OF INSPECTOR GENERAL

http://www.oig.hhs.gov/

The mission of the Office of Inspector General (OIG), as mandated by Public Law 95-452, as amended, is to protect the integrity of the Department of Health and Human Services (HHS) programs, as well as the health and welfare of beneficiaries served by those programs. This statutory mission is carried out through a nationwide network of audits, investigations, and inspections conducted by the following operating components:

Office of Audit Services

The OIG's Office of Audit Services (OAS) provides all auditing services for HHS, either by conducting audits with its own audit resources or by overseeing audit work done by others. Audits examine the performance of HHS programs and/or its grantees and contractors in carrying out their respective responsibilities and are intended to provide independent assessments of HHS programs and operations in order to reduce waste, abuse, and mismanagement and to promote economy and efficiency throughout the Department.

Office of Evaluation and Inspections

The OIG's Office of Evaluation and Inspections (OEI) conducts short-term management and program evaluations (called inspections) that focus on issues of concern to the Department, the Congress, and the public. The findings and recommendations contained in the inspections reports generate rapid, accurate, and up-to-date information on the efficiency, vulnerability, and effectiveness of departmental programs.

Office of Investigations

The OIG's Office of Investigations (OI) conducts criminal, civil, and administrative investigations of allegations of wrongdoing in HHS programs or to HHS beneficiaries and of unjust enrichment by providers. The investigative efforts of OI lead to criminal convictions, administrative sanctions, or civil monetary penalties. The OI also oversees State Medicaid fraud control units which investigate and prosecute fraud and patient abuse in the Medicaid program.

Office of Counsel to the Inspector General

The Office of Counsel to the Inspector General (OCIG) provides general legal services to OIG, rendering advice and opinions on HHS programs and operations and providing all legal support in OIG's internal operations. The OCIG imposes program exclusions and civil monetary penalties on health care providers and litigates those actions within the Department. The OCIG also represents OIG in the global settlement of cases arising under the Civil False Claims Act, develops and monitors corporate integrity agreements, develops model compliance plans, renders advisory opinions on OIG sanctions to the health care community, and issues fraud alerts and other industry guidance.

EXECUTIVE SUMMARY

PURPOSE

To assess how well the Food and Drug Administration manages its new drug application review process.

BACKGROUND

The Food and Drug Administration (FDA) receives new drug applications (NDAs) from sponsors, typically pharmaceutical companies, and reviews these applications for scientific evidence pertaining to the safety and efficacy of drugs. Based on its assessments, the FDA determines whether drugs can be marketed in the United States.

The Prescription Drug User Fee Act (PDUFA), enacted in 1992, authorized FDA to collect user fees from sponsors to help speed up the review of NDAs. It also established time goals for FDA's reviews. In 1997, the FDA Modernization Act reauthorized user fees for another 5 years. It shortened the time goals and called for FDA to work more collaboratively with sponsors. In June 2002, the Public Health Security and Bioterrorism Preparedness Act of 2002 once again reauthorized user fees. The part of this Act addressing user fees is referred to as PDUFA III.

This inquiry focuses on FDA's Center for Drug Evaluation and Research (CDER), which reviews NDAs. This inquiry does not assess the scientific merit of the decisions that FDA has made. Instead, it examines how well FDA carries out its NDA review process. This report draws heavily on the opinions of CDER officials. We surveyed CDER reviewers, receiving an estimated 47 percent response rate (N=401) and interviewed about 80 CDER officials, including managers. In addition, we surveyed sponsors, receiving a 60 percent response rate (N=72), reviewed files for all 15 new molecular entities approved by CDER in fiscal year (FY) 2001, analyzed CDER data regarding the number of advisory committees, observed 17 CDER meetings, interviewed 20 stakeholders, and reviewed relevant FDA policies and procedures. We also drew on data from an internal survey conducted by CDER of a random sample of 188 reviewers that had a 72 percent response rate.

We conducted this inquiry prior to the implementation of PDUFA III. Where appropriate, we indicate the potential impact of PDUFA III on our findings.

FINDINGS

FDA's new drug application review process has several strengths that contribute significantly to its effectiveness.

Both FDA reviewers and sponsors have confidence in the decisions FDA makes. Our review underscored that FDA's NDA review process is science-based and comprehensive. This is supported by the comments of both FDA reviewers and sponsors. Seventy-eight percent of FDA respondents and 86 percent of sponsors indicated in our surveys that they were confident in the decisions FDA makes with regard to a drug's efficacy.

FDA is highly responsive to the time goals required under the Prescription Drug User Fee Act and the FDA Modernization Act. In 1993, median total approval time for CDER was 27 months for standard NDAs classified as new molecular entities; in 2001, it was 19 months. The reduction in approval times helps to ensure timely access to new medications that can benefit the public health.

FDA works collaboratively with sponsors. In FY 2001, CDER conducted 1,021 formal meetings with sponsors. In these meetings, FDA provides valuable advice to sponsors that can help speed up the drug development process.

FDA has taken numerous steps to improve efficiency and consistency. In 2000, CDER issued about 40 guidance documents, most of which it directed to sponsors. Between 1996 and 2001, CDER issued about 140 policies to help guide reviewers. It also now accepts applications electronically.

FDA relies on expert scientific reviewers. Both sponsors and reviewers agreed that FDA's in-house expertise is a key asset of the review process. Funds from user fees have allowed FDA to increase the number of employees for drug reviews by about 700 employees over the past 10 years.

But workload pressures increasingly challenge the effectiveness of the review process.

Reviewers are under constant pressure to meet time goals. They not only review NDAs, but also other key documents submitted by sponsors, some of which also have time goals attached. At the same time, reviewers must provide advice to sponsors and stay abreast of the latest scientific advances in their fields. Below, we present the consequences of these workload pressures.

Reviewer concerns about time pressures. Forty percent of FDA survey respondents who had been at FDA at least 5 years indicated that the review process had worsened during their tenure in terms of allowing for in-depth, science-based reviews. Respondents cited lack of time as the main reason. According to 58 percent of FDA respondents, the allotted 6 months for a priority review is inadequate. This is considerably higher than the 25 percent of respondents who indicated that the allotted 10 months for a standard review is inadequate.

Reviewer concerns about time constraints do not necessarily mean that there is a threat to public health. We have no evidence of a public health concern nor did we seek to obtain such evidence. Reviewers commented in interviews that they did not believe that they were ignoring key information or data contained in the applications in order to meet time goals. The FDA has also received the 4th highest composite score out of the 13 operating divisions within the Department of Health and Human Services on the 2002 Secretary's Quality of Work Life Survey on Organizational Climate, which indicates a positive work environment. However, our survey data do indicate a significant management issue warranting attention.

The PDUFA III should help to address reviewers' concerns about time pressures, as CDER estimates hiring close to 300 additional employees over the next 5 years with funds from user fees.

Less use of advisory committees. Advisory committees are comprised of independent scientific experts who provide advice to FDA during the review process. The number of advisory committee meetings CDER held for NDAs decreased from 40 in 1998 to 23 in 2001. Although the declining number of NDAs submitted by sponsors has contributed in part to this decline, FDA managers also pointed out that they have little time to hold these meetings.

Insufficient time for raising scientific disputes. Pressure to meet time goals may inhibit the raising of disputes. Reviewers may be reluctant to raise disputes due to concerns about slowing down the process. Twenty-one percent of FDA respondents indicated that the work environment allowed for the expression of differing scientific opinions to a small or no extent.

Contributing to staff turnover. The FDA data show that medical officers and pharmacologists had the highest attrition rates within CDER for FY 2001, 8.4 percent and 6.9 percent respectively, compared to the overall rate of 5.5 percent. On an internal CDER survey, 50 percent of reviewers who responded indicated that their workloads are influential reasons to consider leaving FDA.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.