

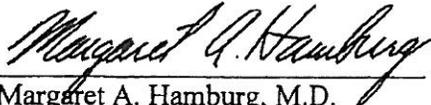
REPORT TO CONGRESS

THIRD ANNUAL REPORT ON DELAYS IN APPROVALS OF
APPLICATIONS RELATED TO CITIZEN PETITIONS AND
PETITIONS FOR STAY OF AGENCY ACTION
FOR FISCAL YEAR 2010

REQUIRED BY SECTION 914 OF THE FOOD AND DRUG
ADMINISTRATION AMENDMENTS ACT

PUBLIC LAW 110-85

Department of Health and Human Services
Food and Drug Administration

 Date JUN 23 2011
Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs

I. STATUTORY REQUIREMENT

The Food and Drug Administration Amendments Act (FDAAA) was enacted on September 27, 2007. Section 914 of Title IX of FDAAA took effect on the date of enactment and amended section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355) by adding new subsection (q). Section 505(q) applies to certain petitions that request the Food and Drug Administration (FDA) take any form of action related to a pending drug application submitted under section 505(b)(2) or 505(j) of the FD&C Act and governs the manner in which these petitions are treated.¹

Section 505(q)(3) of the FD&C Act states that:

The Secretary shall annually submit to the Congress a report that specifies –

- (A) the number of applications that were approved during the preceding 12-month period;
- (B) the number of such applications whose effective dates were delayed by petitions referred to in [505(q)(1) of the FD&C Act] during such period;
- (C) the number of days by which such applications were so delayed; and
- (D) the number of such petitions that were submitted during such period.

FDA is submitting this report to satisfy the obligations set forth in section 505(q)(3).

II. BACKGROUND

A. Citizen Petitions and Petitions for Stay of Agency Action

A citizen petition is a vehicle that stakeholders outside of FDA can use to ask FDA “to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action” (21 CFR 10.25 and 10.30). Pursuant to the governing regulations, petitioners can request, for example, that the agency:

- Disapprove a drug product application;
- Add warnings to a drug’s label; or
- Change products from prescription to over-the-counter (OTC) status.

FDA regulations also provide for the submission of petitions for “stay of action” to delay the effective date of an administrative action, such as the approval of a certain

¹ In this report, an application submitted under section 505(b)(2) of the FD&C Act is referred to as a *505(b)(2) application*, and an application submitted under section 505(j) of the FD&C Act is referred to as an *abbreviated new drug application (ANDA)*.

drug application (21 CFR 10.35). Both citizen petitions and petitions for stay of agency action will be collectively referred to as “petitions” throughout this report, and petitions subject to section 505(q) of the FD&C Act will be referred to as “505(q) petitions.”

B. Delays of Approvals

Section 505(q)(1)(A), together with section 505(q)(5), describe the general scope of section 505(q). Section 505(q)(1)(A) provides:

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

- (i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and
- (ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.²

In section 505(q)(5), the term *application* is defined as an application submitted under section 505(b)(2) or 505(j) of the FD&C Act, and the term *petition* is defined as a request described in section 505(q)(1)(A)(i) (*i.e.*, a written request submitted in accordance with 21 CFR 10.30 or 10.35).

If FDA determines, based on a petition requesting action on a pending ANDA or 505(b)(2) application, that a delay of approval of a pending application is necessary to protect the public health, FDA is required to provide to the applicant, not later than 30 days after making the determination, the following information:

- Notification that the determination has been made;
- If applicable, any clarification or additional data that the applicant should submit to the petition docket to allow FDA to review the petition promptly; and
- A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.³

At FDA’s discretion, the information described above is to be conveyed to the applicant either in a written document or through a meeting with the applicant.⁴ The

² This sentence was added as a technical correction to FDAAA in Public Law 110-316, 122 Stat. 3509, 3524, section 301, enacted August 14, 2008.

³ Section 505(q)(1)(B).

⁴ Section 505(q)(1)(C).

information conveyed as part of the notification is to be considered part of the application and subject to applicable disclosure requirements.⁵

III. INFORMATION REPORTED

Section 505(q)(3) of the FD&C Act requires FDA to submit an annual report to Congress containing certain statistical information regarding the approval of ANDAs and 505(b)(2) applications and the effect, if any, that 505(q) petitions have had on the timing of such approvals. This annual report complies with the statutory reporting requirements for fiscal year 2010, based on data from October 1, 2009, through September 30, 2010.

The statute requires the following information to be included in the report:

- The number of ANDAs and 505(b)(2) applications approved during the reporting period;
- The number of such applications that were delayed by 505(q) petitions;
- The number of days by which such applications were so delayed; and
- The number of 505(q) petitions that were submitted during the reporting period.

During the FY 2010 reporting period, the agency approved 29 505(b)(2) applications and 426 ANDAs. No 505(b)(2) approvals were delayed because of the filing of a 505(q) petition. One ANDA approval was delayed by nine days because of a pending 505(q) petition. Twenty 505(q) petitions were filed during the reporting period. FDA did not miss the statutory deadline for responding to any 505(q) petitions during this reporting period.

FDA's decision to delay the approval of one pending ANDA by nine days was based on the agency's assessment that further review of the issues raised in the 505(q) petition was required to fully assess the petitioners' arguments against approval. FDA was concerned that if it approved the ANDA before resolving the issues raised in the petition and later concluded that one or more of the arguments against approval were meritorious, then the presence on the market of drug products that did not meet the requirements for approval could negatively affect the public health. Thus, FDA decided to delay approval of the product at issue for an additional nine days to complete its analysis of the petition. After FDA completed its review, the agency determined that further delay of approval of the ANDA was not necessary to protect the public health, and the agency approved the ANDA prior to issuing a response to the petition.

IV. IMPLEMENTATION DISCUSSION

FDA has been implementing the provisions of section 505(q) for approximately three years. We did so both by issuing draft guidance to encourage industry to use the 505(q) process appropriately and by reviewing and responding to the more than 70 505(q) petitions that have been filed during the three-year period.

⁵ Section 505(q)(1)(D).

A. Guidance

In January 2009, the agency issued a draft guidance for industry titled: *Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act*. This draft guidance addresses the agency's current thinking on the following topics:

- How FDA determines whether a particular petition would delay approval of a pending ANDA or 505(b)(2) application and, therefore, would fall within section 505(q);
- How FDA interprets the certification and verification requirements under section 505(q); and
- The relationship between the review of petitions and the review of pending ANDAs and 505(b)(2) applications for which FDA has not yet made a decision on approvability.

FDA plans to finalize this guidance in 2011.

B. Petition Review and Observations

During fiscal years (FY) 2008 through 2010, FDA received a total of 72 505(q) petitions (21 in FY 2008, 31 in FY 2009, and 20 in FY 2010). Over this three year period, FDA responded to all but two 505(q) petitions within the 180-day statutory timeframe. In certain circumstances, FDA has responded to 505(q) petitions earlier than required by the statutory timeframe to avoid unnecessary delays in product approval.

FDA continues to monitor the number and nature of 505(q) petitions filed and to analyze whether section 505(q) is effectively discouraging petitioners from submitting petitions primarily to delay the approval of ANDAs or 505(b)(2) applications. FDA also is closely monitoring the effect of 505(q) petitions, and the 180-day statutory response period for these petitions, on the other work of the agency. FDA has consistently met the statutory deadlines by redirecting efforts that otherwise would have been directed to other work, including responding to other citizen petitions. Although we now have three years of experience implementing section 505(q), we do not believe that the data are sufficient to determine whether section 505(q) is having its intended effect.

Some of the trends in 505(q) petitions that we believe may be relevant are as follows:

- Over the three year period during which we have been reviewing 505(q) petitions, the number of applications that have been delayed due to analysis of the issues raised in the 505(q) petitions is low: 4 ANDAs and no 505(b)(2) applications.

- FDA continues to receive 505(q) petitions from ANDA and 505(b)(2) applicants, and not solely from innovator companies.
- In many instances, the statutory deadline for responding to a 505(q) petition occurs before any related ANDAs or 505(b)(2) applications are ready for approval.
- FDA has received serial 505(q) petitions, frequently from the same petitioner, about the same specific drug or class of drugs, sometimes requiring several separate responses about different aspects of the same product. In the current reporting period, for example, the agency received its fourth 505(q) petition relating to the approval of ANDAs for the anti-depressant venlafaxine hydrochloride. These submissions were spread out over a period of 24 months (with filing dates of May 2008, July 2009, August 2009, and May 2010), and each petition raised different scientific issues. The agency responded to all four petitions within the 180-day statutory deadline. Responding to such serial petitions requires the use of substantial FDA resources, on a repeated basis, over a protracted period of time.
- Since the passage of FDAAA, FDA has seen an increase in petitions for reconsideration of the agency's denial of 505(q) petitions, requiring the agency to readdress issues that already have been decided.

As noted above, FDA believes that additional experience and trend data are required to determine whether section 505(q) is accomplishing the stated goals of the legislation. Based on the petitions that we have seen to date, however, the agency is concerned that section 505(q) may not be discouraging the submission of petitions that do not raise valid scientific issues and are intended primarily to delay the approval of competitive drug products. We also believe that innovator companies may be implementing strategies to file serial 505(q) petitions and petitions for reconsideration in an effort to delay approval of ANDAs or 505(b)(2) applications for competing drugs. We will continue to monitor and analyze the 505(q) landscape and will provide further analysis in our next annual report.