

REPORT TO CONGRESS

Fourth Annual Report on Delays in Approvals of
Applications Related to Citizen Petitions and
Petitions for Stay of Agency Action
for Fiscal Year 2011

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

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 that 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 the labeling of a drug; and/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 certain 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

¹ In this report, an application submitted in accordance with 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)*.

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), describes 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 abbreviated new drug application (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

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 FD&C Act, section 505(q)(1)(B).

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 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 (FY) 2011, based on data from October 1, 2010, through September 30, 2011.

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.

Between September 27, 2007 and September 30, 2011, FDA determined that a delay in approving an ANDA was necessary to protect the public health in the case of 5 ANDAs with related 505(q) petitions. FDA has not delayed approval of any 505(b)(2) applications based on 505(q) petitions.

During the FY 2011 reporting period, the agency approved 43 applications submitted under section 505(b)(2) and 458 ANDAs. No 505(b)(2) approvals were delayed because of the filing of a 505(q) petition in this reporting period. One ANDA approval was delayed by 78 days because of pending 505(q) petitions.

FDA's decision to delay the approval of one pending ANDA during this reporting period was based on the agency's assessment that further review of the issues raised in the 505(q) petitions 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 petitions 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 public health. Thus, FDA decided to delay approval of the product at issue for 78 days to complete its analysis of the issues raised in the petitions. 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 on the same day a response to the petitions was issued. This delay had no impact on the marketing of the product because, as a result of a

⁴ FD&C Act, section 505(q)(1)(C).

⁵ FD&C Act, section 505(q)(1)(D).

court's patent decision, the holder of the ANDA is enjoined from marketing the product for several years.

During the FY 2011 reporting period, 20 petitions considered 505(q) petitions were submitted to the agency. FDA did not miss the statutory deadline for responding to any 505(q) petitions during this reporting period.

IV. IMPLEMENTATION DISCUSSION

FDA has been implementing the provisions of section 505(q) for approximately 4 years. FDA has done so both by issuing guidance to encourage industry to use the 505(q) process appropriately and by reviewing and responding to the more than 90 petitions subject to section 505(q) that have been filed during the 4-year period.

A. Guidance.

In January 2009, the agency issued 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*. In June 2011 FDA issued the final guidance (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079353.pdf). The final 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.

B. Petition Review and Observations

During FY 2008 through FY 2011, FDA received a total of 92 petitions subject to section 505(q) (21 in FY 2008, 31 in FY 2009, 20 in FY 2010, and 20 in FY 2011). Over this 4-year period, FDA responded to all but 2 of the 505(q) petitions within the 180-day statutory timeframe that was applicable during that period.⁶ In certain circumstances FDA responded to 505(q) petitions earlier than required by the statutory time frame to avoid unnecessary delays in product approval. As an example, in October 2010 FDA received a petition regarding generic versions of

⁶ The 180-day statutory timeframe for responding to 505(q) petitions was reduced to 150 days by section 1135 of the Food and Drug Administration Safety and Innovation Act.

Xyzal. The petitioner requested that FDA refrain from granting final approval for any ANDA for a generic version of Xyzal (levocetirizine dihydrochloride) if the ANDA includes proposed labeling that omits or carves out Xyzal’s indications for seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR). On February 24, 2011, FDA responded to the petition before the statutory deadline of April 13, 2011. As mentioned in the response, on the same day FDA approved two ANDAs for chronic idiopathic urticaria with labeling that did not include information about the use of Xyzal for the PAR and SAR indications.

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 is also closely monitoring the effect of 505(q) petitions, and the statutory response period for these petitions, on the other work of the agency; FDA consistently met the statutory deadlines by redirecting efforts that otherwise would have been directed to other work, including responding to other citizen petitions.

It is difficult to determine whether section 505(q) is discouraging the filing of citizen petitions aimed at blocking generic competition. However, since the passage of FDAAA, the number of 505(q) petitions submitted annually has been steady – in 3 out of 4 fiscal years, FDA received approximately 20 such petitions:

<u>FY</u>	<u>No. of Petitions</u>	<u>No. of 505(q) petitions</u>	<u>% of 505(q)/all petitions</u>
'08	78	21	26.92
'09	81	31	38.27
'10	76	20	26.32
'11	96	20	20.83

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

- 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. Accordingly, a relatively small percentage of applications are delayed by these petitions.
- Over the 4-year period during which FDA has been reviewing 505(q) petitions, approximately 5% of the petitions resulted in a delay in approving an ANDA.
- FDA continues to receive 505(q) petitions from ANDA and 505(b)(2) applicants, and not solely from innovator companies.

- 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 addition, petitioners are raising their arguments serially, rather than asserting all available arguments in the first petition filed. In the FY 2011 reporting period, for example, the agency received its fourth 505(q) petition relating to the approval of ANDAs for topical ophthalmic products and a third 505(q) petition related to Doryx (doxycycline). The various submissions raised different scientific issues, requiring serial review of different arguments, rather than one comprehensive review of all pertinent arguments. The agency responded to all of these petitions within the statutory deadline. Responding to such serial petitions requires the use of substantial FDA resources, on a repeated basis, over a protracted period of time.

FDA will continue to gain additional experience and monitor trend data in the FY 2012 reporting period to assist Congress in determining whether section 505(q) is accomplishing the stated goals of the legislation. Based on the petitions that FDA has 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. Though many 505(q) petitions do not necessarily raise issues that are important to the public health, the statute requires FDA to prioritize these petitions above other matters, such as safety petitions, that do raise important public health concerns. FDA also believes 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. FDA remains concerned about the resources required to respond to 505(q) petitions within the statutory deadline at the expense of completing the other work of the agency.