Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Elizabeth Giaquinto Friedman 240-402-7930.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

January 2019
Procedural

Contains Nonbinding Recommendations

Draft — Not for Implementation

Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format

Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

January 2019
Procedural

TABLE OF CONTENTS

Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended to assist holders of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) approved under section 505(c) and 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(c) and (j)), respectively, with submission of marketing status notifications required under section 506I of the FD&C Act (21 U.S.C. 356i). This guidance identifies the required content for these marketing status notifications and the format by which these notifications should be submitted to the Agency.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (Hatch-Waxman Amendments) specifically required FDA to publish and make publicly available, among other things, a list of drug products either approved under section 505(c) of the FD&C Act for safety and effectiveness or approved under section 505(j) of the FD&C Act.[2] FDA fulfills these requirements in its publication, *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[3]

[1] This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research at the Food and Drug Administration.

[2] See section 505(j)(7)(A) of the FD&C Act.

[3] The Orange Book is available at https://www.accessdata.fda.gov/scripts/cder/ob/.

The Orange Book contains different drug product lists, including the "Prescription Drug Product List," the "Over-the-Counter (OTC) Drug Product List," and the "Discontinued Drug Product List."[4] The Prescription Drug Product and OTC Drug Product Lists are sometimes referred to as the *active* section of the Orange Book, and the Discontinued Drug Product List is sometimes referred to as the *discontinued* section of the Orange Book. The discontinued section of the Orange Book sets forth, among other items, drug products (1) that have been identified by the application holder as not being marketed or (2) whose marketing has been discontinued for reasons other than safety or effectiveness, as determined by FDA.[5] When FDA learns that any such drug product is not being marketed, FDA, based on its long-standing practice, moves that drug product from the active section of the Orange Book to the discontinued section of the Orange Book.[6]

FDA regulations require NDA and ANDA holders to notify the Agency of the marketing status of drug products approved under NDAs and ANDAs.[7] The FDA Reauthorization Act of 2017[8] (FDARA) added section 506I to the FD&C Act, which imposes additional marketing status reporting requirements as follows:

- ***Notification of withdrawal from sale*** — requires NDA and ANDA holders to provide a written notification to FDA 180 days prior to withdrawing an approved drug from sale[9]

- ***Notification of drug not available for sale*** — requires NDA and ANDA holders to provide a written notification to FDA within 180 days of the date of approval of a drug if that drug will not be available for sale within 180 days of the date of approval[10]

- ***One-time report on marketing status*** — required NDA and ANDA holders to provide a written notification to FDA within 180 days of enactment of FDARA[11] stating whether the NDA and ANDA holder's drug(s) in the active section of the Orange Book were available for sale or if one or more of the NDA or ANDA holder's drugs in the active section had been withdrawn from sale or had never been available for sale.[12]

[4] See the Orange Book Preface (38th ed., 2018) at vi.

[5] See id.

[6] See id. at xxiv.

[7] See, e.g., 21 CFR 314.81(b)(2)(ii)(*a*) and 314.81(b)(3)(iv).

[8] Public Law 115-52.

[9] Section 506I(a) of the FD&C Act. The statute further states that if a submission under section 506I(a) is not practicable 180 days before withdrawing the product from sale, that submission should be made "as soon as practicable but not later than the date of withdrawal" from sale.

[10] Section 506I(b) of the FD&C Act.

[11] FDARA was enacted on August 18, 2017. This one-time report was due to FDA on Wednesday, February 14, 2018.

[12] Section 506I(c) of the FD&C Act.

In considering whether a drug product has been withdrawn from sale, FDA notes that the Agency has previously indicated that withdrawal from sale is not limited to a permanent withdrawal of a product but can also include "any decision to discontinue marketing of [that] product."[13] In particular, FDA has described its policy on determining whether a product is considered to have been "withdrawn from sale" as follows:

> For purposes of section[] 505(j)(5) and 505(j)(6)(C) of the [FD&C Act], a drug shall be considered to have been 'withdrawn from sale' if the applicant has ceased its own distribution of the drug, whether or not it has ordered recall of previously distributed lots of the drug. A routine, temporary interruption in the supply of a drug product would not be considered a withdrawal from sale, however, unless triggered by safety or effectiveness concerns.[14]

Likewise, FDA has considered a drug product to have been withdrawn from sale if the applicable NDA or ANDA holder has notified FDA that the drug product is not being marketed.[15]

Section 506I of the FD&C Act requires FDA to update the Orange Book "based on the information provided" by NDA and ANDA holders in these three marketing status notifications "by moving drugs that are not available for sale from the active section to the discontinued section of [the Orange Book], except that drugs [that are determined to] have been withdrawn from sale for reasons of safety or effectiveness shall be removed from [the Orange Book] in accordance with subsection 505(j)(7)(C)."[16] Also, section 506I of the FD&C Act authorizes FDA to move the NDA and/or ANDA holder's (or holders') drug products from the active section of the Orange Book to the discontinued section if an NDA or ANDA holder fails to submit any of these three marketing status notifications.[17]

III. CONTENT AND FORMAT OF MARKETING STATUS NOTIFICATIONS

The subsequent subsections of this guidance provide information on submitting the marketing status notifications required under section 506I of the FD&C Act to FDA.[18] For each of these notifications, the notification may serve as its own cover letter (i.e., no separate cover letter is needed).

A. Notification of a Withdrawal From Sale

[13] See "Abbreviated New Drug Application Regulations," final rule, 57 FR 17950 at 17956 (April 28, 1992).

[14] "Abbreviated New Drug Application Regulations," proposed rule, 54 FR 28872 at 28907 (July 10, 1989).

[15] Orange Book Preface (38th ed., 2018) at xxiv.

[16] Section 506I(e) of the FD&C Act.

[17] Section 506I(d) of the FD&C Act.

[18] Please note that changes to drug product listings that fall outside the scope of this guidance (e.g., a change in ownership or a name change) should be submitted via correspondence to the approved application.

A notification of a withdrawal from sale must include:

1. The National Drug Code(s) under which the drug is listed (21 CFR part 207)
2. The established name of the drug
3. The proprietary name of the drug, if applicable
4. The NDA or ANDA number
5. The strength of the drug
6. The date on which the drug is expected to no longer be available for sale
7. The reason for the withdrawal[19]

The applicant should submit a notification of a withdrawal from sale in a letter to the applicable NDA or ANDA file through the electronic submissions gateway.[20] The notification should prominently identify the submission as an "**ADMINISTRATIVE CHANGE / NOT AVAILABLE FOR SALE.**" This letter does not replace an application holder's obligation to submit a separate written request under 21 CFR 314.150(c) if it is seeking a voluntary withdrawal of its approved application.

B. Notification of a Drug Not Available for Sale

A notification that a drug is not available for sale within 180 days of the date of approval of the drug must include:

1. The established name of the drug
2. The proprietary name of the drug, if applicable
3. The NDA or ANDA number
4. The strength of the drug
5. The date on which the drug will be available for sale, if known
6. The reason for not marketing the drug after approval[21]

The applicant should submit a notification that a drug will not be available for sale in a letter to the applicable NDA or ANDA file through the electronic gateway. The notification should prominently identify the submission as an "**ADMINISTRATIVE CHANGE / NOT AVAILABLE FOR SALE.**"

Once marketing begins, FDA recommends that the NDA or ANDA holder notify FDA of the commenced marketing in a letter to the applicable NDA or ANDA file through the electronic gateway" to ensure that appropriate changes can be made in the Orange Book. The notification

[19] Section 506I(a) of the FD&C Act.

[20] The electronic submissions gateway is available at https://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/. Questions related to electronic submissions should be emailed to the CDER Electronic Submission (ESUB) Team at esub@fda.hhs.gov.

[21] Section 506I(b) of the FD&C Act. Examples of reasons for not marketing the drug after approval that may be provided in this notification include, but are not limited to, a lack of demand, a license agreement, an interruption in the supply of drug product components, or issues related to production for a commercial launch at day 180.

should prominently identify the submission as an "**ADMINISTRATIVE CHANGE / NOTIFICATION OF COMMERCIAL MARKETING.**"

C. One-Time Report on Marketing Status[22]

Under section 506I(c) of the FD&C Act, all holders of approved NDAs and ANDAs were required to submit a one-time report on the marketing status of their drug products in the active section of the current edition of the Orange Book by February 14, 2018. This one-time written report was required to indicate whether:

1. All of the NDA or ANDA holder's drugs in the active section of the Orange Book were available for sale

2. One or more of the NDA or ANDA holder's drugs in the active section of the Orange Book had been withdrawn from sale or had never been available for sale

This report was required to include the information required under section 506I(a) or 506I(b) of the FD&C Act, as applicable, for each relevant drug product that had been withdrawn from sale or had never been available for sale.[23]

[22] FDA also created a web page, available at https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ApprovedDrugProductswithTherapeuticEquivalenceEvaluationsOrangeBook/ucm590216.htm, that provided information on how NDA and ANDA holders could submit one-time report information to FDA.

[23] Id.