

Post-Approval Notice Requirements

Andrew Coogan, PharmD, BCPS

Office of Generic Drug Policy

Office of Generic Drugs

U.S. Food and Drug Administration

Agenda

- Review Section 506I of the FDA Reauthorization Act of 2017 (FDARA)
- Discuss reporting requirements for applicants
- Provide a summary of 506I(b) compliance
- Identify ways for applicants to provide more useful information to FDA

FDARA Overview



FDARA was signed into law August 18, 2017



Allowed for the continuation of generic drug user fees for another 5-year reauthorization cycle (FY2018 to FY2022)



Amended laws for improved generic drug access



Made changes to reporting requirements

Sec. 506I

Prompt Reports of Marketing Status

(a) 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

(b) 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

(c) 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 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Orange Book were available for sale or if one or more of the NDA or ANDA holder's drugs in the active section had been withdrawn from sale or had never been available for sale

Notification of Drug not Available for Sale

- Notification must include:
 - The established name of the drug
 - The proprietary name of the drug, if applicable
 - The NDA or ANDA number
 - The strength of the drug
 - The date on which the drug will be available for sale, if known
 - The reason for not marketing the drug after approval

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

Excerpt from Final Approval Letter

Notification of Drug not Available for Sale

- Notice must be submitted within 180 days of the date of approval
- Notice should be submitted in a letter to the applicable ANDA file through the electronic gateway
- The notice should prominently identify the submission as an, “ADMINISTRATIVE CHANGE / NOT AVAILABLE FOR SALE”

Notification of Drug not Available for Sale

Example 1

- ANDA 444444 is approved on March 1, 2020, but due to a settlement agreement with the NDA holder, Applicant plans to launch its product on July 1, 2020
 - No notification required under 506I(b)*

*If this ANDA is a first filer, applicant would be required to submit notice within 30 days of marketing. See 21 CFR 314.107(c)(2).

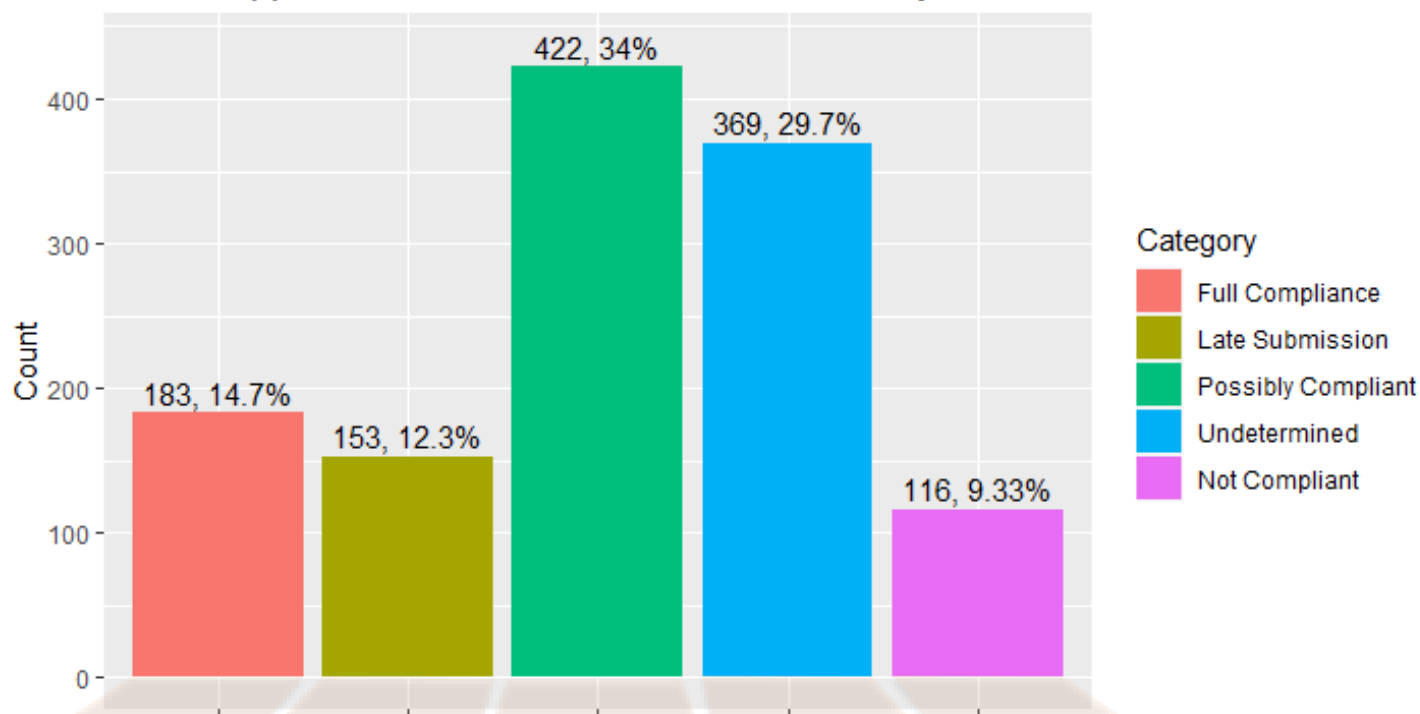
Notification of Drug not Available for Sale

Example 2

- ANDA 555555 is approved on March 1, 2020, but due to a delay in delivery of Active Pharmaceutical Ingredient, commercial batches will not be completed until September 2020
 - Submit notice under 506I(b) with the reason the product will not be available for sale within 180 days of approval and the date it will become available for sale, if known

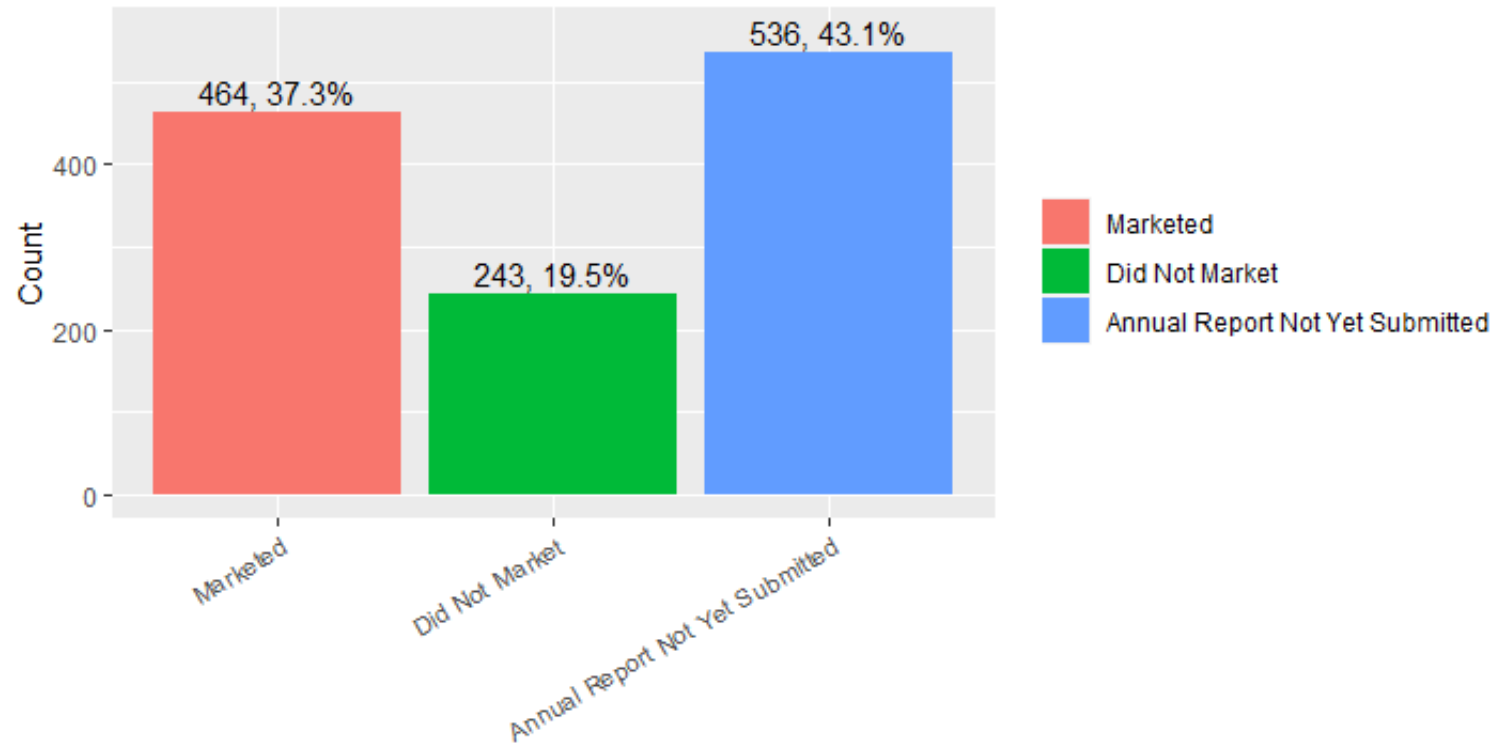
Summary of 506I(b) Compliance

506I(b) Compliance ANDAs approved from October 1, 2017 to February 28, 2019



Compliant	Late Submission	Possibly Compliant	Undetermined	Not Compliant
506I notice or notification of commercial marketing submitted within 180 days of approval	506I(b) notice or Notification of Commercial Marketing submitted after 180 days of approval	No 506I(b) notice but annual report shows product was distributed during the first year after approval	No 506I(b) notice and annual report not yet submitted	No 506I notice and annual report shows product was not distribute during the first year after approval

Marketed within 1 year of approval?
ANDAs approved from October 1, 2017 to February 28, 2019

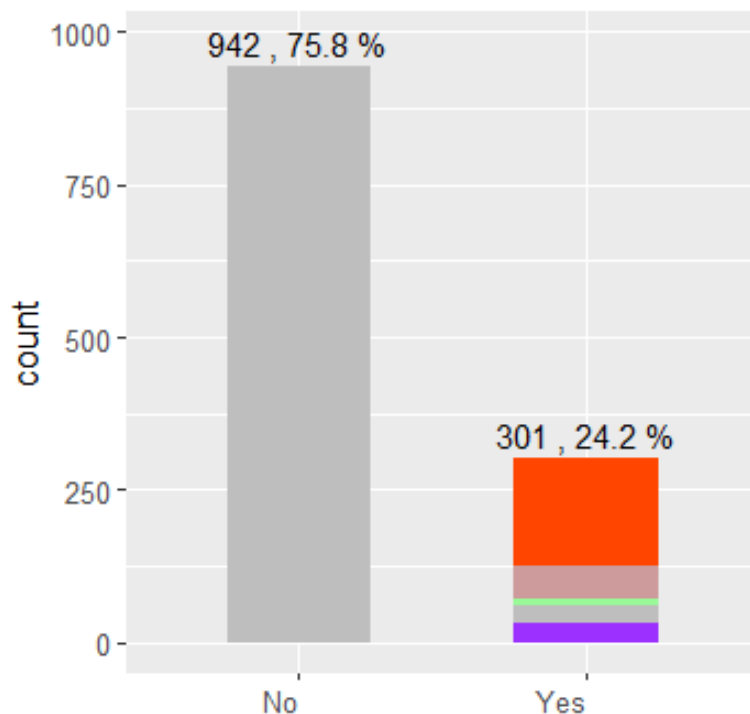


Fiscal year 2018 (October 1, 2017 to September 30, 2018):

- 796 approvals (82 first generics)
- 88% had submitted an Annual Report at time of review
 - 65% of all approvals reported product distribution within first year
 - 64% of first generics reported product distribution within first year

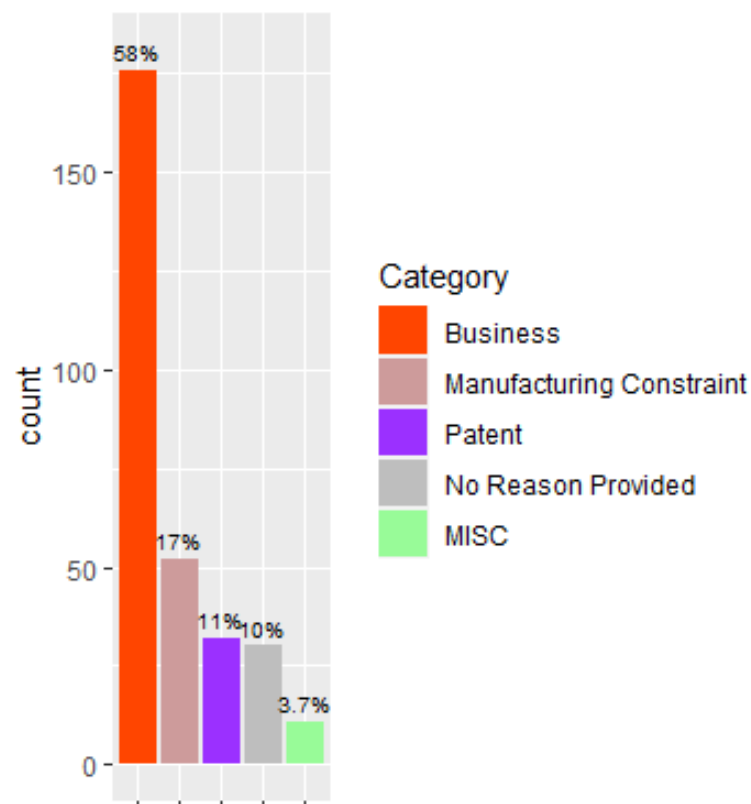
Not marketing within 180 days: Was FDA Notified?

ANDAs approved from October 1, 2017 to
February 28, 2019



Reason for Not Marketing

301 ANDAs with 506I Notification



Business

- Competitive market place
- New customer to be identified
- Launch preparation is on-going
- Delay in identifying a marketing partner

Manufacturing Constraint

- Shortage of Active Pharmaceutical Ingredient (API)
- Production scheduling delay
- Manufacturing facility modification or site change

Patent

- Settlement
- Delay in obtaining or cancellation of license agreement
- Patent protection



Reason for Not Marketing: A Closer Look

Business

- ~70% had no patents listed for the reference listed drug at the time of approval

Manufacturing Constraint

- 27% are API related

Patent

- 55% are first filers

How can applicants provide more useful information to FDA?

- Submit the information in a standardized, consistent format
- Provide more specific dates
 - Instead of 'Calendar Year (CY) 2020', say:
 - February 2020
 - First Quarter of CY 2020
- Expand on the reason
 - Instead of 'Business Reason', say:
 - Business reasons based on competitive market place with X other application holders currently marketing
 - Have another approved ANDA for same substance
 - Identifying marketing partner

506I(a)

- Application holders are also required to submit reports under section 506I(a), Notification of withdrawal from sale, 180 days prior to withdrawing an approved drug from sale
 - Note that a drug is considered withdrawn from sale when the application holder ceases its own distribution, even if the application holder plans to eventually return to the market, so long as the application holder has not ceased distribution due to a routine, temporary interruption in supply
- Further information on the 506I(a) reporting requirement is available in our guidance on 506I marketing status notifications



Key Take-Aways

- If your product will not be available for sale within 180 days of approval, submit notice under 506I(b)
- Providing more information allows FDA to better understand barriers of generic drug entry to the market place after approval
- Remember to also report on withdrawals from sale under 506I(a)

Link to Guidance:

[Guidance for Industry: Marketing Status
Notifications Under Section 506I of the
Federal Food, Drug, and Cosmetic Act](#)

Questions?

CDER-OGDPET@fda.hhs.gov

OrangeBook@fda.hhs.gov

