180-Day Exclusivity

SBIA 2020: Celebrating 40 Years: An In-Depth Examination of the FDA Orange Book

Session 11: Orange Book Exclusivity Part III - 180-Day and CGT Exclusivities

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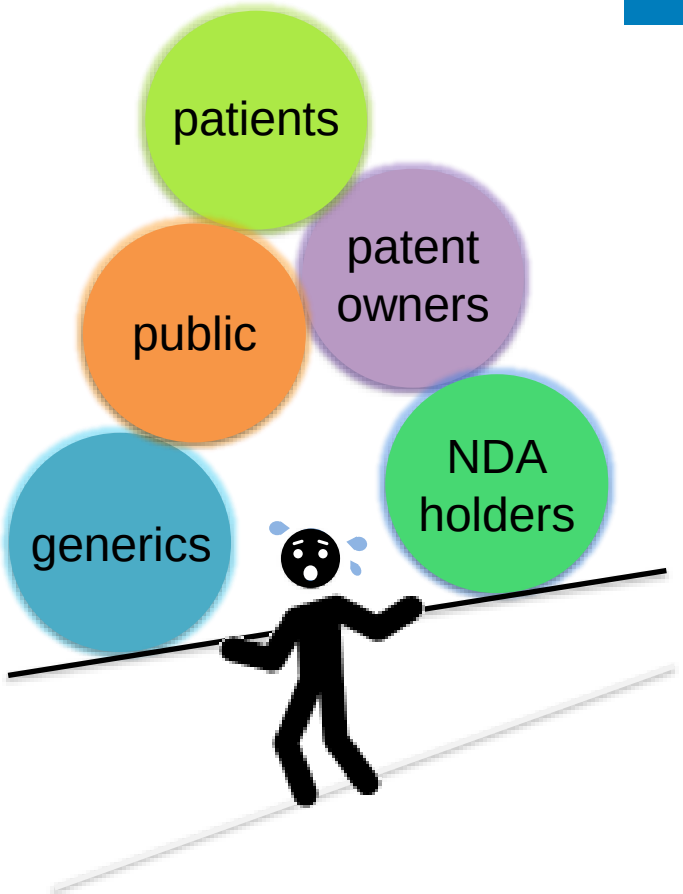
Learning Objectives

- Discuss context and eligibility for 180-day exclusivity
- Discuss forfeiture of 180-day exclusivity
- Describe some mechanics of 180-day exclusivity
- Discuss resources for 180-day exclusivity

180-day Exclusivity: Context

- ANDA approval pathway as we know it was created by the Drug Price Competition and Patent Term Restoration Act of 1984
  - Further amended by Medicare Prescription Drug, Improvement, and Modernization Act of 2003
- The Hatch-Waxman Amendments seek to balance the many interests at stake

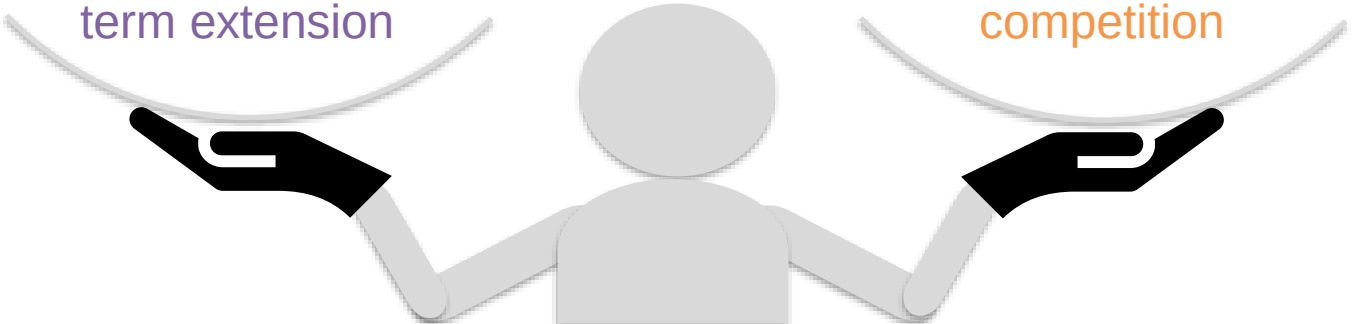


180-day Exclusivity: Context

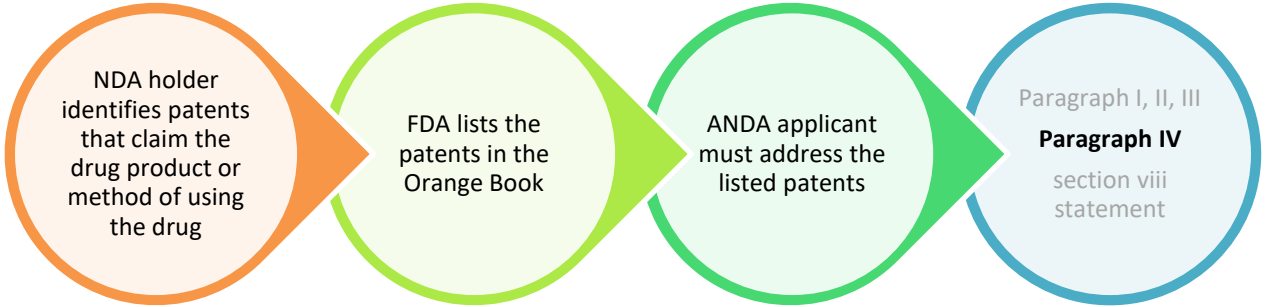
The Hatch-Waxman Amendments seek to balance the many interests at stake

NDA holders may be eligible for regulatory exclusivities or patent term extension

NDA holders are subject to generic competition

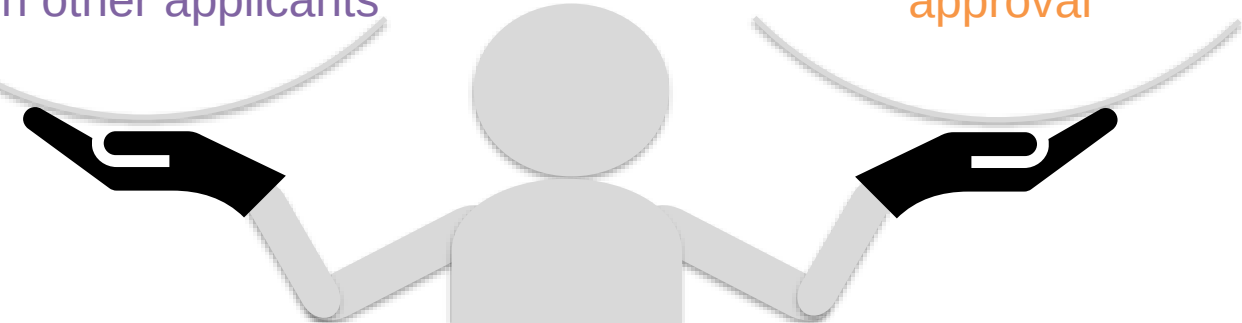


180-day Exclusivity: Context



Being able to market before listed patents expire **180-day exclusivity** vis-à-vis certain other applicants

Patent litigation 30-month stay of ANDA approval



180-day Exclusivity: Eligibility

(iv) 180-DAY EXCLUSIVITY PERIOD.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

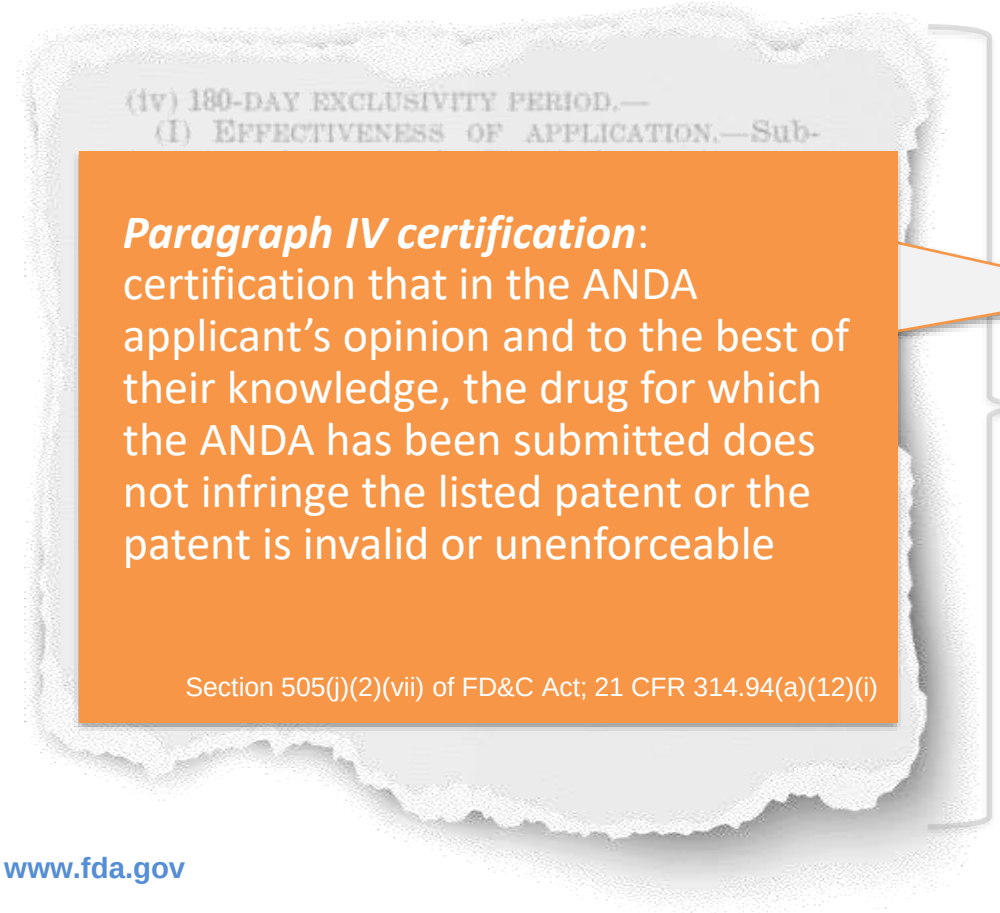
(II) DEFINITIONS.—In this paragraph:

(aa) 180-DAY EXCLUSIVITY PERIOD.—The term ''180-day exclusivity period'' means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

Section 505(j)(5)(B)(iv) of FD&C Act

ANDAs that contain a paragraph IV certification will not be made effective until **180 days after** the date of first commercial marketing of the drug by any first applicant

180-day Exclusivity: Eligibility

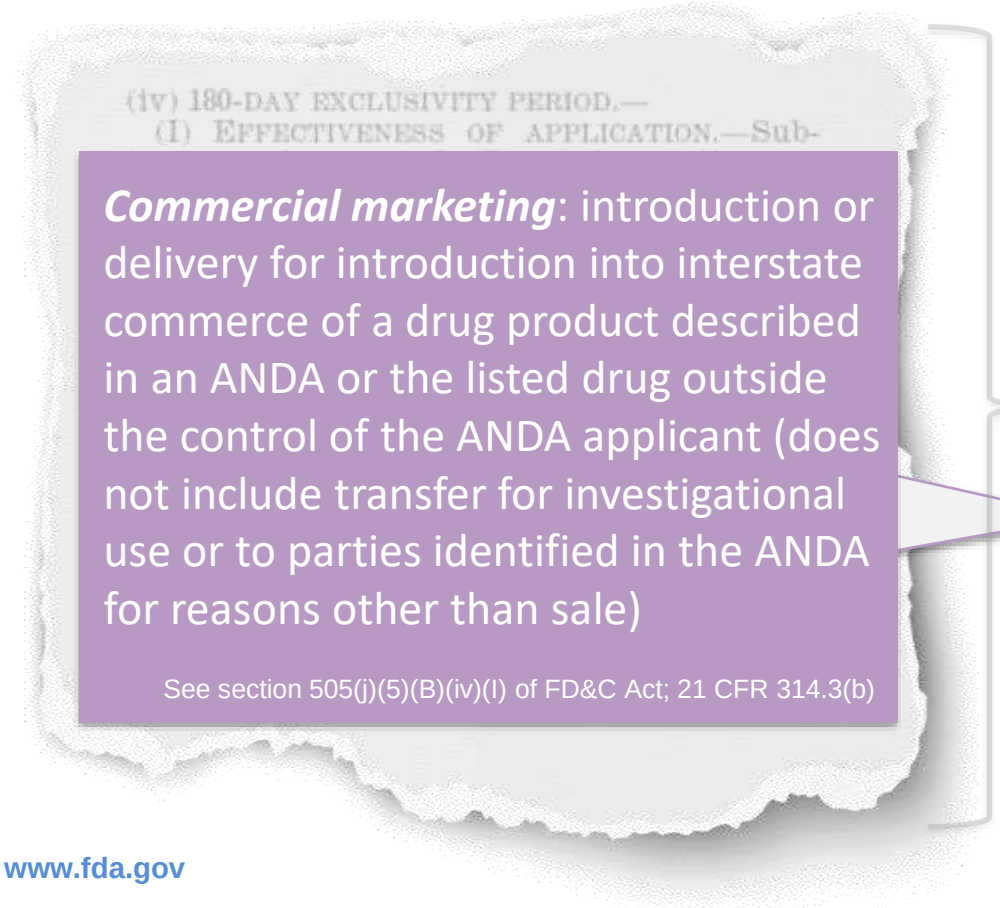


Paragraph IV certification: certification that in the ANDA applicant's opinion and to the best of their knowledge, the drug for which the ANDA has been submitted does not infringe the listed patent or the patent is invalid or unenforceable

Section 505(j)(2)(vii) of FD&C Act; 21 CFR 314.94(a)(12)(i)

ANDAs that contain a paragraph IV certification will not be made effective until **180 days after** the date of first commercial marketing of the drug by any first applicant

180-day Exclusivity: Eligibility



Commercial marketing: introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA or the listed drug outside the control of the ANDA applicant (does not include transfer for investigational use or to parties identified in the ANDA for reasons other than sale)

See section 505(j)(5)(B)(iv)(I) of FD&C Act; 21 CFR 314.3(b)

ANDAs that contain a paragraph IV certification will not be made effective until **180 days after** the date of first commercial marketing of the drug by any first applicant

180-day Exclusivity: Eligibility

First applicant: an applicant that, on the first day on which a substantially complete application containing a paragraph IV certification is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a paragraph IV certification for the drug

Section 505(j)(5)(B)(iv)(II) of FD&C Act

ANDAs that contain a paragraph IV certification will not be made effective until **180 days after** the date of first commercial marketing of the drug by any first applicant

180-day Exclusivity: Eligibility

1

First applicant: an applicant that, on the first day on which a substantially complete application containing a paragraph IV certification is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a paragraph IV certification for the drug

Section 505(j)(5)(B)(iv)(II) of FD&C Act

- More than one substantially complete ANDA with a paragraph IV certification can be submitted on “the first day”

180-day Exclusivity: Eligibility

First applicant: an applicant that, on the first day on which a substantially complete application containing a paragraph IV certification is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a paragraph IV certification for the drug

2

Section 505(j)(5)(B)(iv)(II) of FD&C Act

- ***Substantially complete***: ANDA on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A) of section 505(j)
- Does not contain a deficiency described in 21 CFR 314.101(d) and (e)

180-day Exclusivity: Eligibility

First applicant: an applicant that, on the first day on which a substantially complete application containing a paragraph IV certification is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a paragraph IV certification for the drug

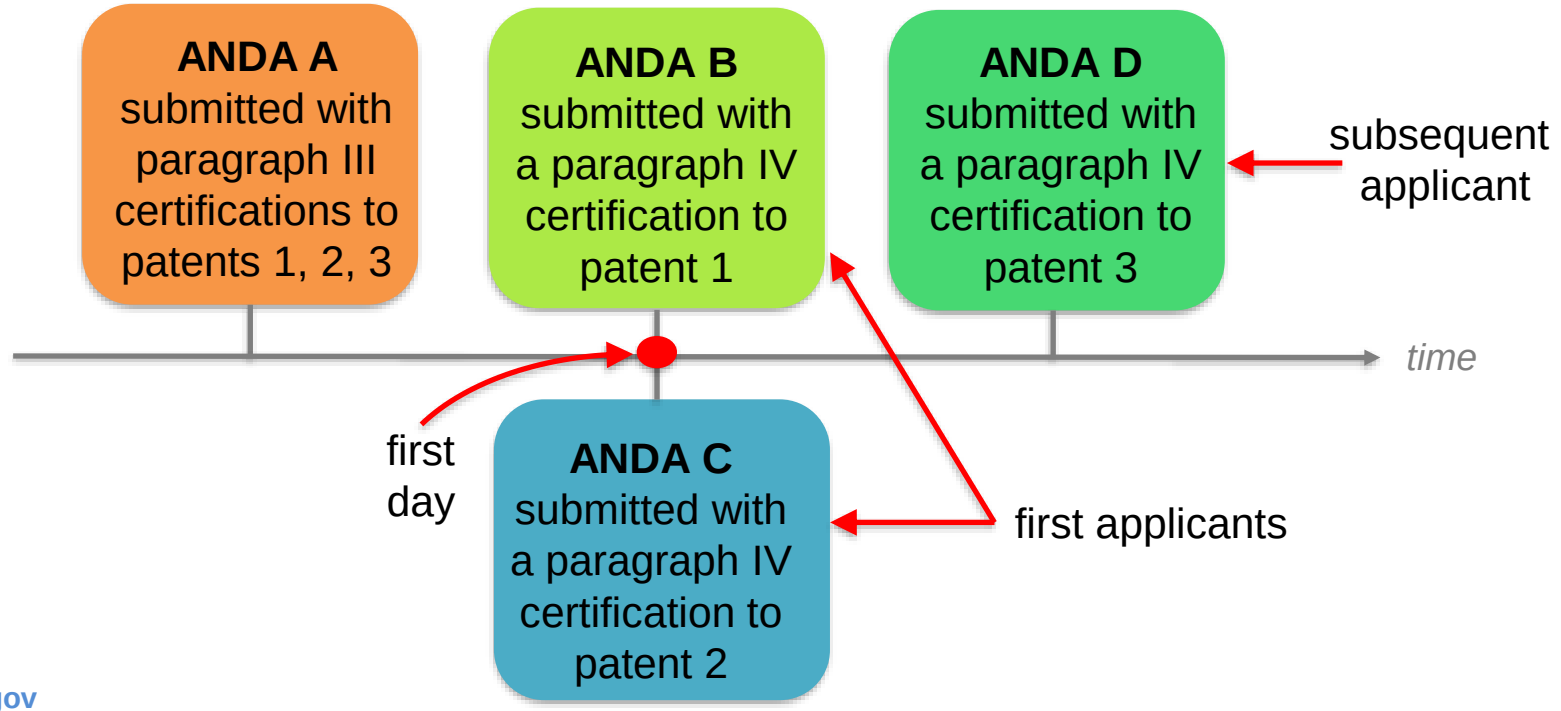
3

Section 505(j)(5)(B)(iv)(II) of FD&C Act

- Only needs to contain one paragraph IV certification
- Can be directed to one or more listed patent
- Can be directed only to the drug substance or drug product claims of a listed patent

180-day Exclusivity: Eligibility

- Orange Book contains three listed patents for RLD X



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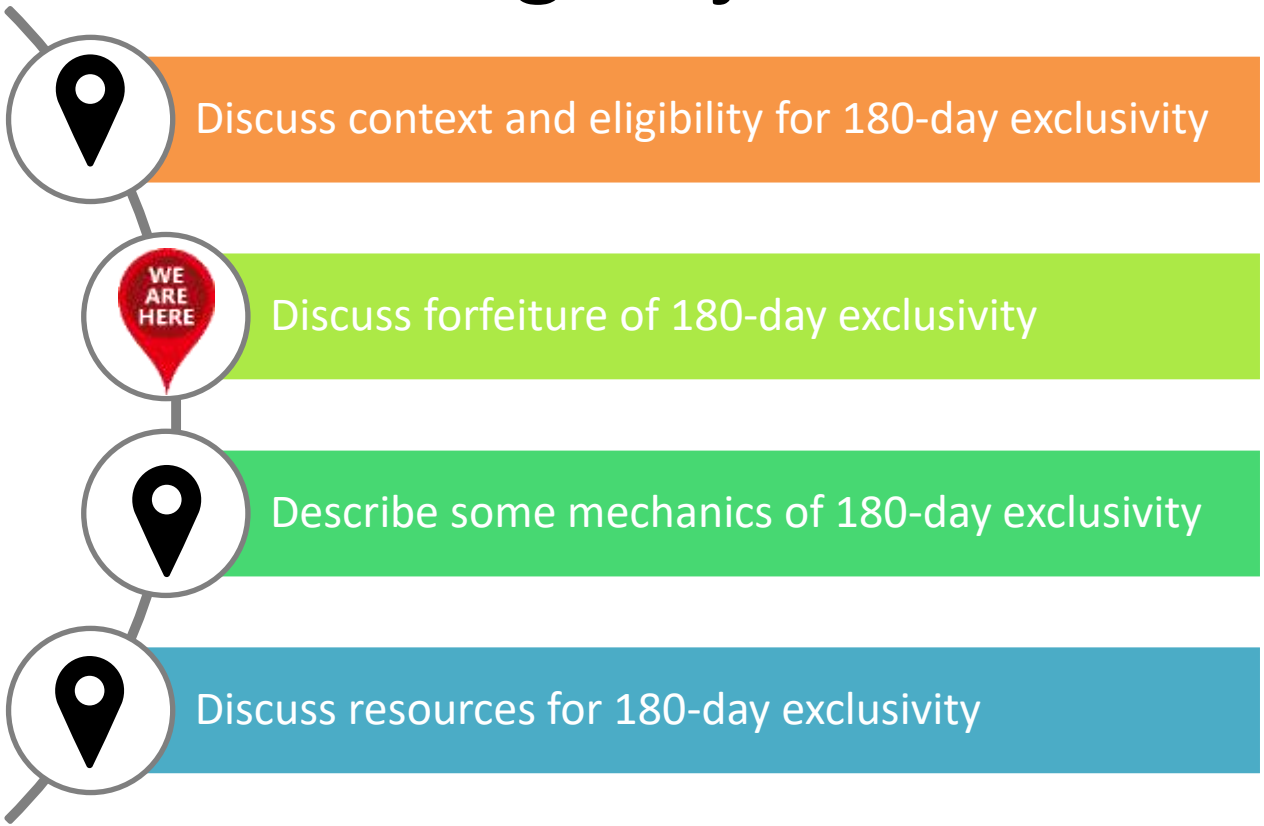
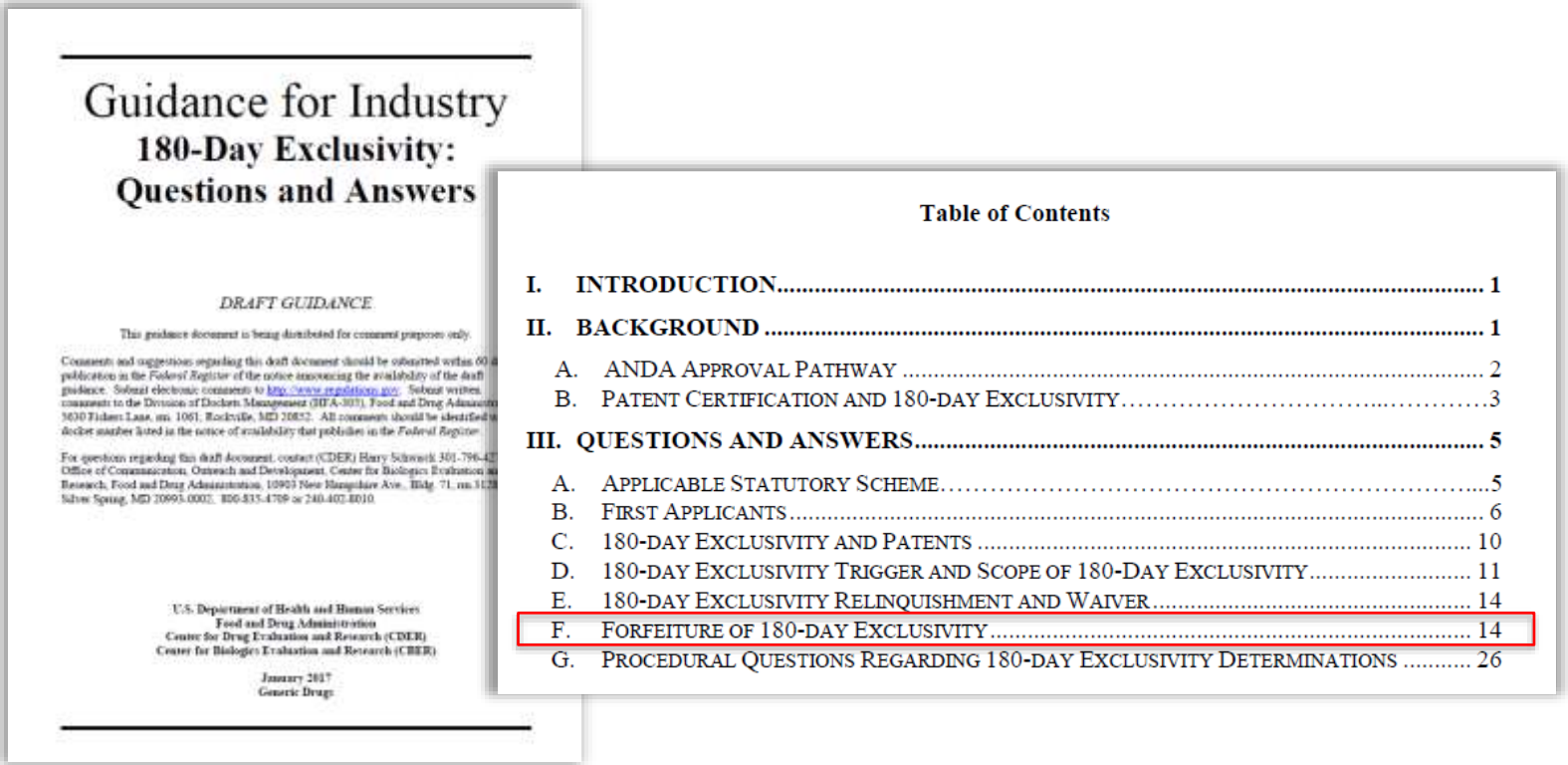


180-day Exclusivity: Forfeiture

1. Failure to market
2. Withdrawal of the ANDA
3. Amendment or withdrawal of qualifying paragraph IV certification(s)
4. Failure to obtain Tentative Approval
5. Agreement with another applicant, NDA holder, or patent owner that violates antitrust laws
6. Expiration of all qualifying paragraph IV-certified patents

See section 505(j)(5)(D) of FD&C Act

180-day Exclusivity: Forfeiture



Guidance for Industry

180-Day Exclusivity: Questions and Answers

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

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

January 2017
Generic Drugs

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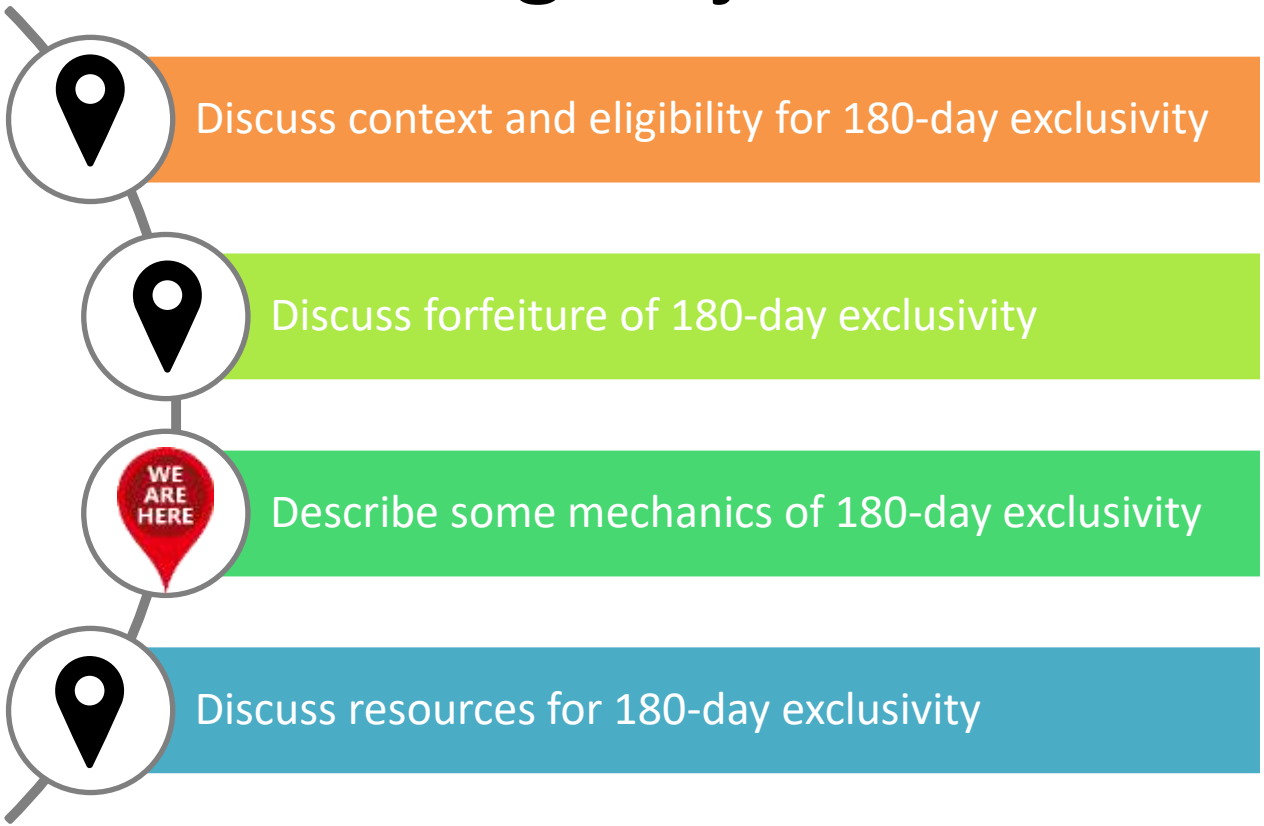
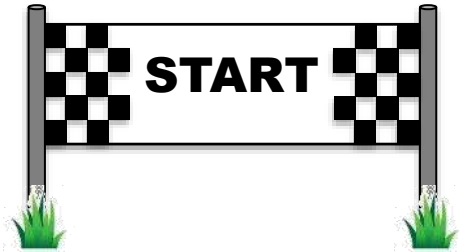


180-day Exclusivity: Mechanics

- Eligibility is determined when an ANDA is otherwise ready for approval
  - Formal determinations may be deferred in certain cases, e.g., no subsequent applicant is ready for approval

180-day Exclusivity: Mechanics

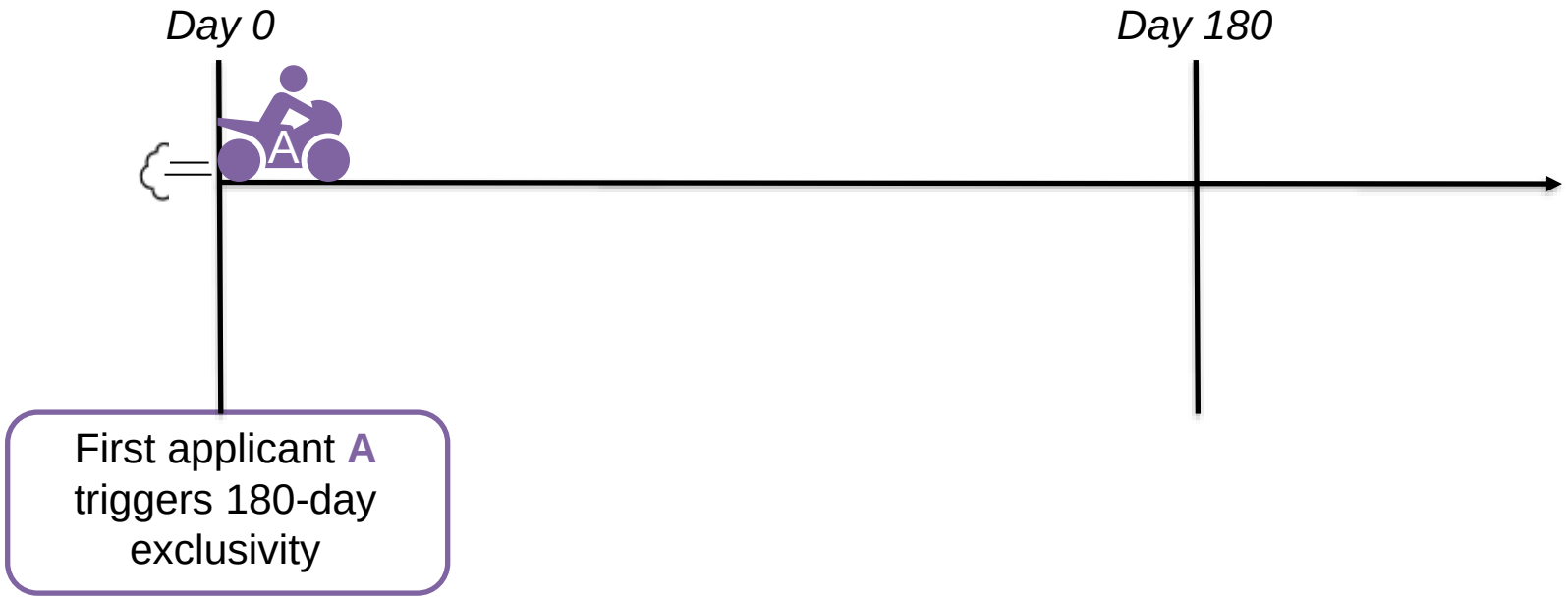
- Starts when any first applicant first commercially markets the ANDA product or the listed drug
  - A first applicant must submit correspondence to its ANDA notifying FDA within 30 days of the date of its first commercial marketing of its drug product or the listed drug



21 CFR 314.107(c)(2)

180-day Exclusivity: Mechanics

- There is one 180-day exclusivity period



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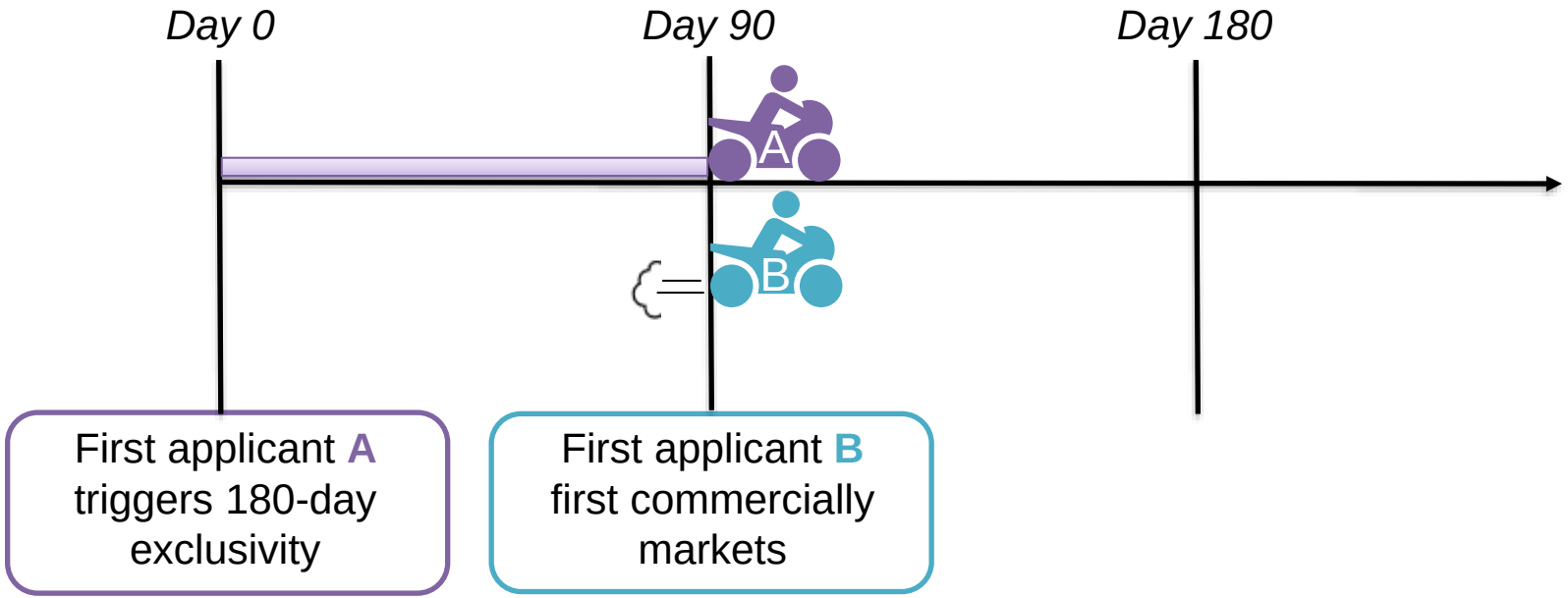

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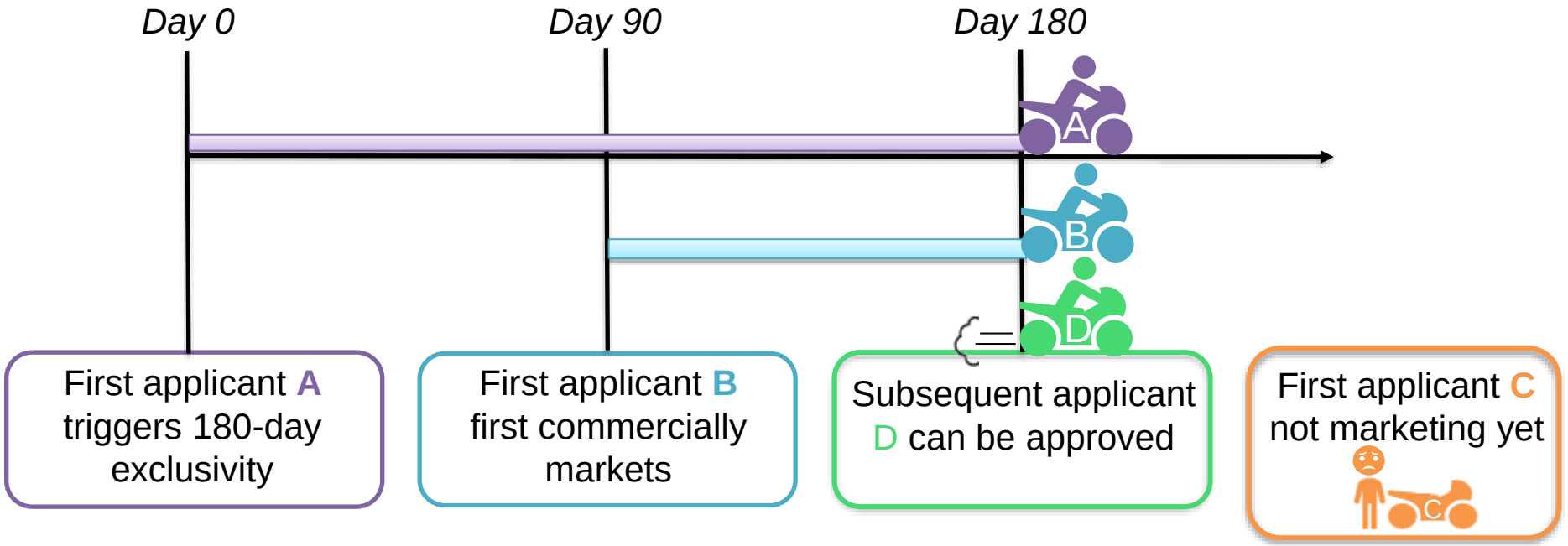


180-day Exclusivity: Mechanics

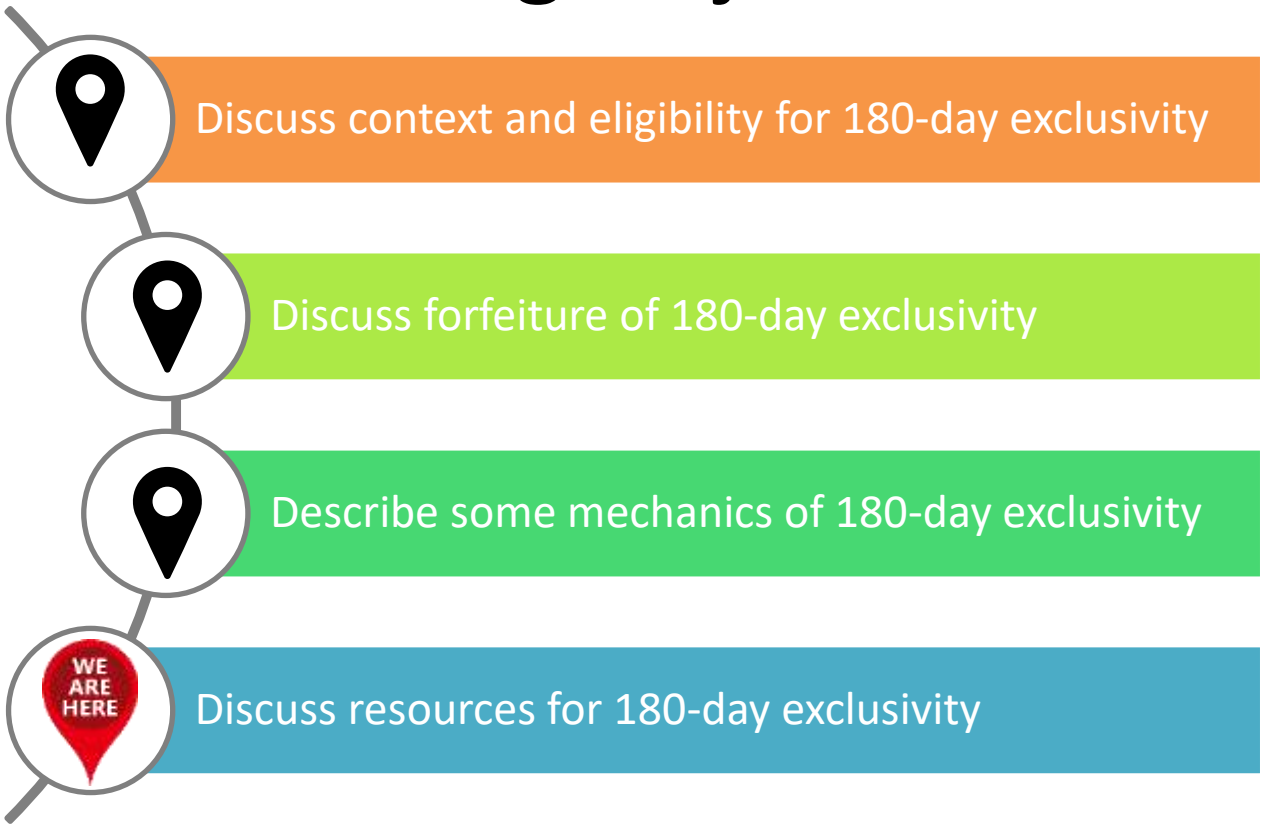
- Blocks approval of a *subsequent applicant*'s ANDA
  - i.e., submitted after the first day, contains a paragraph IV certification

- Does not block authorized generics, other first applicants, or ANDAs with no paragraph IV certifications

180-day Exclusivity: Mechanics

- It can be relinquished or waived
  - Relinquish: first applicant abandons eligibility for 180-day exclusivity
    - If all first applicants relinquish eligibility, subsequent applicants otherwise eligible for approval will be informed their ANDAs may be approved
  - Waive: first applicant permits approval of a particular subsequent applicant's ANDA during the 180-day exclusivity period
    - Only the subsequent applicant(s) in whose favor exclusivity is waived will be informed

Learning Objectives



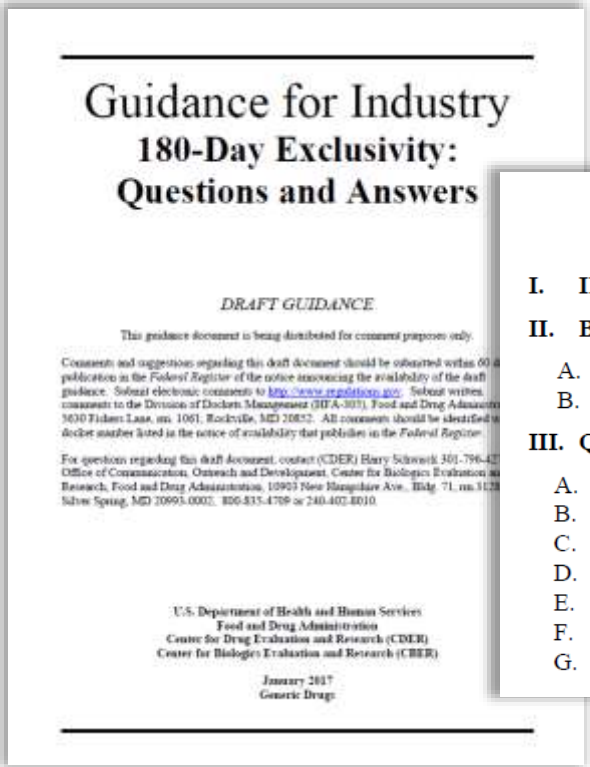
180-day Exclusivity: Resources

- Paragraph IV Certification List

  https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions#List

- ❑ RLD name, NDA number, dosage form, strength
- ❑ Date of first paragraph IV submission
- ❑ Number of potential first applicant ANDAs
- ❑ 180-day decision status
- ❑ Date of first approval of first applicant ANDA
- ❑ Date of first commercial marketing
- ❑ Expiration date of latest-to-expire qualifying patent

180-day Exclusivity: Resources



Guidance for Industry

180-Day Exclusivity: Questions and Answers

DRAFT GUIDANCE

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Comments and suggestions regarding this draft document should be submitted within 60 d
publication in the *Federal Register* of the notice announcing the availability of the draft
guidance. Submit electronic comments to http://www.regulations.gov. Submit written
comments to the Division of Dockets Management (HFA-305), Food and Drug Administr
5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified w
docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Harry Schwenk 301-796-42
Office of Communication, Outreach and Development, Center for Biologics Evaluation a
Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm.3128
Silver Spring, MD 20993-0002; 800-835-4709 or 240-402-8010.

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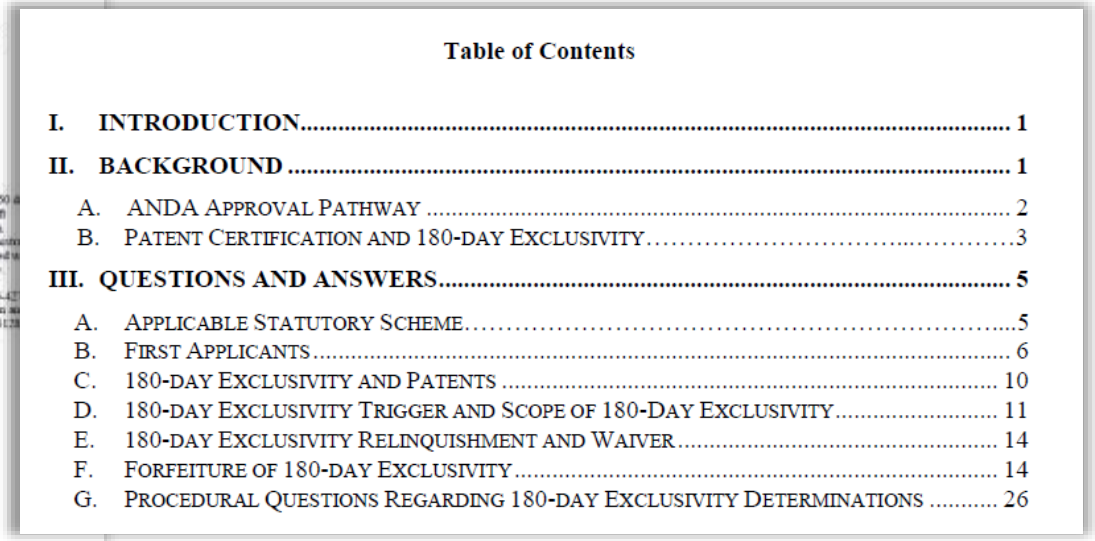
January 2017
Generic Drugs



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Challenge Question #1

The 180-day exclusivity period:

A. Is guaranteed for all first applicants

B. Blocks approval of all ANDAs submitted after the first day

C. Can block approval of subsequent applicants' ANDAs

D. Runs for 180 days after the approval of each first applicant's ANDA

Challenge Question #2

Which of the following statements is NOT true?

A. To be a first applicant, the applicant must submit a paragraph IV certification to each listed patent

B. There can be more than one first applicant

C. There is only one 180-day exclusivity period

D. The 180-day exclusivity period can be forfeited, relinquished, or waived

Summary

- 180-day exclusivity is an incentive for ANDA applicants who expose themselves to the risk of patent litigation
- First applicants are eligible for 180-day exclusivity
- 180-day exclusivity blocks approval of subsequent applicants' ANDAs
- 180-day exclusivity is not guaranteed; it can be forfeited, relinquished, or waived

Questions?

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