of rare diseases. Because of the small size of rare disease populations and global occurrence of rare conditions, it is considered that the networks needed to support rare disease drug development would also have global reach and operations.

II. Requested Information and Comments

FDA requests input on practical steps and successful approaches to startup, implement, and sustain global clinical trials networks, including specific considerations for establishing such networks for a range of rare diseases. Questions that could be addressed include, but are not limited to, those listed below. It is not necessary to answer all the questions below.

1. What should be the immediate (<3 years) and long-term objectives of a global clinical trials network?
2. How could a global clinical trials network for rare disease be organizationally structured (*e.g.,* what mix of scientific and clinical disciplines are engaged to staff it; what process or guidance is followed for study protocol design; what standard procedures are employed for conduct of trials, and related protection of study participants and study data, etc.)? For example:
- Are there experiences that can be shared regarding networks integrating a disease-specific development center with a disease-agnostic operations center?
- Are there experiences that can be shared regarding networks focused on a broad group of rare diseases and collaboration with regional or disease-specific networks?

3. What kind of investigator experience is needed to start up and expand to implement a global clinical trial network (*e.g.,* experience with clinical trial research administration, clinical trial operations, working with pharmaceutical companies in the design, conduct and management of clinical trials)?
4. What are successful models of governance for global clinical trial networks (*e.g.,* role, responsibilities, and composition of various governing bodies)?
5. What are potential opportunities to leverage and/or complement other existing networks (*e.g.,* Institute for Advanced Clinical Trials for Children Network, Duke Clinical Research Institute Pediatric Trial Network, National Institutes of Health (NIH) Rare Diseases Clinical Research Network, NIH Experimental Therapeutics Clinical Trials Network, European Network of Paediatric Research at the European Medicines Agency)?
6. What infrastructure is required to startup, implement, and sustain a global clinical trials network (*e.g.,* required administrative, financial and physical resources, centralized functions, data coordination and network operations, global interoperability)?
7. What level of funding would be needed to establish a network, potentially expand a network, and sustain the network over the long term (*e.g.,* at least 5 years and longer)? A a range of estimates (*e.g.,* startup costs, annual operating costs) and associated assumptions would be helpful.
8. What are the key milestones and associated timelines for starting up and expanding to implement a global clinical trials network?
9. What are potential challenges or barriers to starting up, implementing, and sustaining a global rare disease clinical trials network?

Dated: May 26, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020–11655 Filed 5–29–20; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–N–1069]

Approved Drug Products With Therapeutic Equivalence Evaluations (the ''Orange Book''); Establishment of a Public Docket; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; establishment of a public docket; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the establishment of a public docket to solicit comments on FDA's publication entitled ''Approved Drug Products With Therapeutic Equivalence Evaluations'' (commonly known as the ''Orange Book''). The Orange Book identifies drug products approved by FDA under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and includes related information. As part of FDA's Drug Competition Action Plan and our continued effort to improve transparency and provide useful information to regulated industry and the public, we are seeking comments on how stakeholders and the public use the Orange Book and whether it can be improved.

DATES: Submit either electronic or written comments by August 31, 2020.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:
- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:
- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2020–N–1069 for ''Approved Drug Products With Therapeutic Equivalence Evaluations (the 'Orange Book'); Establishment of a Public Docket; Request for Comments.'' Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.
- Confidential Submissions—To submit a comment with confidential information that you do not wish to be

made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Lisa Bercu, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 1672, Silver Spring, MD 20993, 240–402–6902, *Lisa.Bercu@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

As its core function, the Orange Book identifies drug products approved by FDA under the FD&C Act and includes patent and exclusivity information related to those drug products. The main criteria for the inclusion of a drug product in the Orange Book are that the drug product is the subject of an approved application and that FDA has not determined the drug product to have been withdrawn for safety or efficacy reasons. The Orange Book includes drug products approved prior to the 1962 amendments to the FD&C Act on the basis of safety and found to be effective through the Drug Efficacy Study Implementation process. However, pre-1938 drug products not subject to the premarket approval authorities of the FD&C Act are excluded from the Orange Book. In addition, drug products that were not marketed at the time of the first publication of the Orange Book or were discontinued between 1980 and 1987, prior to the identification of discontinued products, are also not included in the list.

The Orange Book also contains therapeutic equivalence evaluations for approved multisource prescription drug products. *Therapeutic equivalents* are approved drug products that FDA has determined are pharmaceutical equivalents for which bioequivalence has been demonstrated, and can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling (§ 314.3(b) (21 CFR 314.3(b))). The therapeutic equivalence evaluations in the Orange Book serve as public information available to prescribers, pharmacists, Federal and State health agencies, and private formularies, among others, to promote public education in the area of drug product selection and to foster the containment of health care costs. Therapeutic equivalence evaluations in the Orange Book are not official FDA actions affecting the legal status of products under the FD&C Act.

The Orange Book is composed of four main parts: (1) The Prescription Drug Product List, which is a list of approved marketed prescription drug products with therapeutic equivalence evaluations; (2) the OTC Drug Product List, which is a list of marketed over-the-counter (OTC) drug products that have been approved in new drug applications (NDAs) or abbreviated new drug applications (ANDAs); (3) the Drug Products with Approval under section 505 of the FD&C Act (21 U.S.C. 355) administered by the Center for Biologics Evaluation and Research List; and (4) the Discontinued Drug Product List, which is a cumulative list of approved drug products that have never been marketed, are for exportation, are for military use, are not commercially distributed by a Federal or State government entity, have been discontinued from marketing and FDA has not determined that they were withdrawn from sale for safety or effectiveness reasons, or have had their approvals withdrawn for other than safety or efficacy reasons subsequent to being discontinued from marketing. The Orange Book also includes indices of prescription and OTC drug products by proprietary name (brand name or trade name) or, if no proprietary name exists, established name of the active ingredient and by applicant name, which have been abbreviated for this publication. The Addendum to the Orange Book provides patent information for certain listed drugs, and identifies drugs that qualify under the FD&C Act for periods of exclusivity, as described in detail below.

The Orange Book was first published on October 31, 1980. On September 24, 1984, the President signed into law the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98–417) (Hatch-Waxman Amendments), which required that FDA make publicly available a list of approved drug products with monthly supplements (section 505(j)(7)(A) of the FD&C Act). The Orange Book and its monthly Cumulative Supplements satisfy this requirement.

Since that time, the Orange Book has played an essential administrative role in FDA's implementation of the FD&C Act. For example, the FD&C Act requires NDA holders to submit the patent number and expiration date of any patent which claims the drug or a method of using such drug and for which a claim of patent infringement could reasonably be asserted against a person engaged in the unlicensed manufacture, use, or sale of the drug (see section 505(b)(1) and 505(c)(2) of the FD&C Act; see also 21 CFR 314.50(h), 314.53, and 314.70(f)). The FD&C Act requires FDA to publish this patent information (see section 505(b)(1) and 505(c)(2) of the FD&C Act). This patent information submitted by NDA holders is listed in the Orange Book.

In addition, section 505(j)(7)(A)(i)(III) of the FD&C Act requires that FDA publish and make publicly available information to show whether in vitro or in vivo bioequivalence studies, or both studies, are required for ANDAs that refer to an NDA, and FDA has determined that the therapeutic equivalence codes for multisource products in the Orange Book satisfy this requirement.

The Orange Book also identifies drugs that qualify under the FD&C Act for periods of exclusivity. An NDA or ANDA holder is eligible for exclusivity if statutory and regulatory requirements are met. Exclusivities under the FD&C Act include pediatric exclusivity, Generating Antibiotic Incentives Now or GAIN exclusivity, 180-day exclusivity, competitive generic therapy exclusivity, new chemical entity exclusivity, 3-year exclusivity, and orphan drug exclusivity (see sections 505(c)(3)(E), 505(j)(5)(B)(iv), 505(j)(5)(B)(v),

505(j)(5)(F), 505A (21 U.S.C. 355a), 505E (21 U.S.C. 355f), 506H (21 U.S.C. 356h), and 527 (21 U.S.C. 360cc) of the FD&C Act; see also 21 CFR 314.108, 316.31, 316.34). The exclusivities identified above are set forth on a product-specific basis in the Orange Book. This information is used by a wide range of stakeholders, including applicants of ANDAs and 505(b)(2) applications, in planning product development.

The Orange Book also plays an essential administrative role in FDA's implementation of recent statutory provisions related to drug product regulation. For example, section 505(j)(12) of the FD&C Act, added by the FDA Reauthorization Act of 2017 (Pub. L. 115–52) (FDARA), requires FDA to publish on its website and update at least every 6 months a list of approved NDA products that are off-patent and off-exclusivity, and for which FDA has not approved an ANDA referencing that NDA drug product, and FDA uses the Orange Book to populate this list. Section 506I of the FD&C Act requires NDA and ANDA holders to provide a written notification to FDA 180 days prior to withdrawing an approved drug from sale, to provide 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, and to have reviewed information in the Orange Book and submitted a one-time marketing status report. This information is used by FDA to move drugs that are not available for sale from the ''Prescription Drug Product List'' to the ''Discontinued Drug Product List'' in the Orange Book (see section 506I(e) of the FD&C Act).

FDA has historically sought to update and enhance the Orange Book to make it more accessible and useful to regulated industry and the public. Below are examples of updates FDA has made to the publication:

- In 1985, FDA added to the Orange Book a list of OTC drug products that have been approved in NDAs or ANDAs.
- In 1997, FDA published the Orange Book on the internet.
- In 2003, FDA started publishing an indicator as to whether a listed patent contains drug substance and/or drug product claims.
- In 2005, FDA made the Orange Book available for download off the Agency's website.
- In 2005, FDA switched from publishing patent listings in a public docket to publishing them daily in the Orange Book.
- In 2005, FDA switched from publishing generic drug approvals monthly to publishing them daily.
- In 2015, FDA launched a mobile application, ''Orange Book Express,'' to put timely information in the hands of those using smartphones and tablets.
- In 2016, FDA redesigned the Orange Book website to include commonly used features on the home page and to allow users to better navigate the Orange Book and customize their search.
- In 2017, FDA revised the Orange Book so that drug listings now clarify which listed drugs are RLDs and which are reference standards (see § 314.3(b)), as well as to clarify which products in the ''Discontinued Drug Product List'' may be referred to as an RLD.
- In 2017, FDA revised the Orange Book to include listed patent submission dates, when available.
- In 2017, FDA added the patent disputes list to the Orange Book website, which informs stakeholders which patents have been disputed by an outside party to FDA.
- In 2018, FDA updated the Orange Book to include descriptions indicating which indication(s) are protected by orphan drug exclusivity.

As part of FDA's Drug Competition Action Plan [1] and our continued effort to provide more accessible and useful information in the Orange Book, FDA is considering whether there are other opportunities to enhance the publication. The Drug Competition Action Plan aims to facilitate more generic competition, promote patient access, and improve the economics of developing generic medicines. Soliciting public comment on this topic will help guide the Agency's priorities as we consider enhancing the Orange Book.

II. Establishment of a Public Docket and Request for Comments

FDA is establishing a public docket to solicit input from a broad group of stakeholders, including patients, health care providers, drug manufacturers, public policy makers (*e.g.,* Federal and State health agencies), individuals involved in patent litigation (*e.g.,* patent counsel), and any other interested parties, on whether and how the Orange Book can be improved. (To note, FDA intends to publish a separate **Federal Register** notice seeking public input specifically on patent listings in the Orange Book in the near future, and thus is not soliciting comment on that topic now.) In addition to general comments, FDA is interested in responses to the following questions:

- What types of people or entities use the Orange Book?
- What sections of the Orange Book do these different types of people or entities use?
- For what reasons do these people or entities use the Orange Book? What additional information or features (*e.g.,* additional search functions) could be incorporated into the Orange Book to make it more useful?
- Is the information in the Orange Book regarding therapeutic equivalence generally useful?
  - How useful is the second letter of a therapeutic equivalence evaluation code?
  - How could the therapeutic equivalence information be made more user-friendly or otherwise be tailored to meet the needs of people or entities that use the Orange Book (*e.g.,* the therapeutic equivalence evaluation code)?
  - If you use the information regarding therapeutic equivalence, how do you use it?
  - Does the information regarding therapeutic equivalence promote drug competition? And if so, how?
- Is there any other information regarding the Orange Book that would be useful for FDA to consider?

Dated: May 26, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020–11683 Filed 5–29–20; 8:45 am]

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[1] Available at *https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan.*

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–D–1068]

Orange Book—Questions and Answers; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Orange Book—Questions and Answers.'' This guidance is intended to assist interested parties (including prospective drug product applicants, drug product applicants, and approved application holders) in utilizing the *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the