agency stated ''that it is at least theoretically possible.'' [18]

That was not always the case. For many years, FDA acknowledged that at least some drugs are not ''new drugs'' subject to FDA approval prior to marketing. In a 1980 version of the *Orange Book,* FDA stated that ''[t]he law also permits drugs to be legally marketed without such fully approved applications under certain circumstances,'' including ''drugs marketed prior to 1938 that are not subject to the pre-market clearance procedures of the law'' and ''drug products marketed between 1938 and 1962 that were approved for safety but not effectiveness.'' [19] In the same publication, the agency went on to identify specific products, noting ''commonly used large volume intravenous products are not included on the List [of FDA-approved drugs] (*e.g.,* dextrose 5% with water, dextrose 10% with water, sodium chloride 0.9% injection),'' since ''all of these drug products came on the market in glass containers before 1938 and have not been required to obtain an approved new drug application as a condition of marketing.'' [20] In the 2000 edition of the *Orange Book,* FDA cited to the barbiturate ''Phenobarbital Tablets'' as an example of ''pre-1938 drugs.'' [21] The 2011 Guidance, issued absent notice-and-comment rulemaking and without prior public comment, contains no acknowledgement of these prior positions.[22]

This evolution in the agency's thinking has had consequences. Under the UDI, FDA required the manufacturer of an epinephrine brand which originally came onto the market in 1901 to submit an NDA.[23] The drug colchicine, a product FDA acknowledged ''was available in oral dosage form during the 19th century,'' [24] was also approved through the UDI. The interpretation of the definition of ''new drug'' espoused in the 2011 Guidance essentially foreclosed the possibility that these two century-old drugs were pre-1938 grandfathered drugs exempt from the approval process. The 2017 study discussed above found that the average wholesale unit price of epinephrine and colchicine increased by 58.3% and 3,323.5%, respectively,[25] costs absorbed by American patients and taxpayers.

The regulatory history of the prescription drug Daraprim raises similar issues. FDA originally approved Daraprim (pyrimethamine) for safety in 1953, and later deemed the drug effective through the Drug Efficacy Study Implementation, or DESI review process.[26] The drug is listed on the World Health Organization's *List of Essential Medications,* ''a list of minimum medicine needs for a basic health-care system, listing the most efficacious, safe and cost-effective medicines for priority conditions.'' [27] In 2015, the company Turing Pharmaceuticals ''raised the price [of the drug] to $750 a tablet from $13.50, bringing the annual cost of treatment for some patients to hundreds of thousands of dollars.'' [28] Turing came by this windfall, at least in part, because of FDA's interpretation of the definition of ''new drug'' in the FD&C Act as articulated in the 2006 and 2011 Guidances, a view that foreclosed the possibility that Daraprim, a drug more than sixty years old, could ever qualify as GRASE. That position effectively prevented other manufacturers of generic versions of this product from entering the market without an approved abbreviated new drug application, allowing Turing to enjoy a single-source position in the marketplace while potential competitors went through the regulatory process. In February 2016, Congress held a hearing on this widely-publicized issue. Ultimately, FDA approved a generic competitor for this single-source drug in February 2020.

The Department wishes to engage with the public on the contours of the exceptions to the definition of ''new drug.'' In this regard, HHS is reviewing whether certain drugs, including the drug subject to Congressional scrutiny in 2016, might qualify as exempt from the FDA approval requirement. To aid that effort, HHS asks for input from patients, health care providers, industry, and other stakeholders to provide information responsive to any of the topics below:

1. Lists of drugs marketed prior to June 25, 1938 that are currently available on the market.

2. The extent to which drugs marketed prior to June 25, 1938, or drugs that might qualify as GRASE, have regulatory approvals in countries outside the United States.

3. Whether there would be adverse clinical or economic consequences to deeming as GRASE those drugs previously approved by the FDA for which patent and regulatory exclusivity have expired.

4. Any published literature reviews or clinical studies related to any drugs potentially exempt from the new drug approval requirement.

Dated: November 20, 2020.

Alex M. Azar II,

Secretary, Department of Health and Human Services.

[FR Doc. 2020–26133 Filed 11–24–20; 8:45 am]

BILLING CODE 4150–26–P

[18] *Id.* at 12 (emphasis in original).

[19] FDA, *Approved Prescription Drug Products with Therapeutic Equivalence Evaluations* (herein the *Orange Book*), at I–3 (1st ed. 1980).

[20] *Id.* at I–13.

[21] *Id.* at I–13. FDA, *Orange Book,* at v (2000); *see also* FDA, *Orange Book,* at iv (29th ed. 2009) (containing same reference to ''pre-1938 drugs'' and phenobarbital tablets). FDA included a reference to ''pre-1938 drugs'' like phenobarbital tablets in the *Orange Book* as late as 2016, FDA, *Orange Book,* at iv (36th ed. 2016), but removed the reference in its 2017 edition and subsequent versions.

[22] *Cf. F.C.C.* v. *Fox Television Stations, Inc.,* 556 U.S. 502, 515 (2009) (''To be sure, the requirement that an agency provide reasoned explanation for its action would ordinarily demand that it display awareness that it *is* changing position.'')

[23] FDA, Ctr. For Drug Evaluation and Research, Application Number: 204200Origs1s000, 204200Orig2s000, Summary Review, at 3, *https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/204200Orig1Orig2s000SumR.pdf.*

[24] 75 FR 60768 (Oct. 1, 2010).

[25] Gupta, *supra* note 7, at 1072; *see also* Aaron S. Kesselheim and Daniel H. Solomon, *Incentives for Drug Development—The Curious Case of Colchicine,* N. Engl. J. Med. 362;22 at 2046 (noting the dramatic rise in the price of Colchicine after implementation of the UDI, but that ''there is no evidence of any meaningful improvement to the public health'' from the regulatory changes).

[26] 36 FR 14662, 14662–63 (Aug. 7, 1971).

[27] World Health Organization, *20th WHO Model List of Essential Medications,* at 24 (Mar. 2017).

[28] Andrew Pollack, *Drug Goes From $13.50 a Tablet to $750, Overnight,* N.Y. Times, Sept. 20, 2015, *https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html.*

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2010–D–0529]

Qualification Process for Drug Development Tools; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration's (FDA or Agency) Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) are announcing the availability of a final guidance for industry and FDA staff entitled ''Qualification Process for Drug Development Tools.'' Under the 21st Century Cures Act (Cures Act), enacted on December 13, 2016, a new section was added to the Federal Food, Drug, and Cosmetic Act (FD&C Act), which defined a three-stage qualification process for drug development tools (DDTs). This guidance meets the Cures

Act's requirement to issue guidance on this qualification process. It elaborates on the new qualification process and transparency requirements and discusses the taxonomy for biomarkers and other DDTs. This guidance finalizes the draft guidance of the same title issued on December 16, 2019.

DATES: The announcement of the guidance is published in the **Federal Register** on November 25, 2020.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time 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–2010–D–0529 for ''Qualification Process for Drug Development Tools.'' Received comments 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, 240–402–7500.

- 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, 240–402–7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Chris Leptak, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6461, Silver Spring, MD 20993–0002, 301–796–0017; or Stephen Ripley, Center for Biologics Evaluation and Research, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002; 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

CDER and CBER are announcing the availability of a final guidance for industry and FDA staff entitled ''Qualification Process for Drug Development Tools.'' Signed into law on December 13, 2016, the Cures Act codified, in new section 507 of the FD&C Act (21 U.S.C. 357), a new statutory process for DDT qualification and added transparency provisions for information related to qualification submissions through which there is enhanced ability to share knowledge. In addition, Congress directed the establishment of a taxonomy for the classification of biomarkers (and related scientific concepts) for use in drug (including biological product) development. CDER and CBER convened a public meeting on December 11, 2018, to solicit public input about implementing the new qualification process under section 507 of the FD&C Act and about identifying the Biomarkers, EndpointS, and other Tools (BEST) glossary as the taxonomy for classifying types of DDTs, including biomarkers. CDER and CBER are issuing this final guidance to meet the Cures Act requirement that the Agency issue final guidance on the section 507 qualification process.

DDTs are methods, materials, or measures that can aid drug development and regulatory review. Qualification means that a DDT and its proposed context of use can be relied upon to have a specific interpretation and application in drug development and regulatory review. Qualified DDTs can accelerate the integration of innovation, clinical knowledge, and scientific advances, thereby expediting drug development and aiding the regulatory review of applications.

Although the DDT qualification process is voluntary, requestors who seek qualification under section 507 of the FD&C Act must follow the three-

stage process described in the Cures Act. This consists of the following stages: The Letter of Intent, the Qualification Plan, and the Full Qualification Package. These stages are discussed in detail in section III of the final guidance.

The Cures Act includes transparency provisions that require the Agency to make information with respect to qualification submissions publicly available. A description of information that is made public on the Agency's website is provided in section II of the final guidance.

CDER and CBER have considered public comments made during the December 11, 2018, public meeting and submitted to the docket in developing the draft guidance of the same title published on December 16, 2019 (84 FR 68460). The Agency received various comments to the docket in response to the publication of the draft guidance and has considered those comments in developing this final guidance. Changes made in the final guidance in response to comments include requests for additional clarity on the qualification process, support for the proposed time frames, and requests to reference specific programs' content element outlines in the guidance. This final guidance meets the Cures Act's requirement to finalize guidance on the section 507 qualification process and affirms the BEST glossary as the taxonomy for classifying types of DDTs. This guidance does not address evidentiary standards for purposes of DDT qualification. It also does not address the qualification of medical device development tools or other programs under the Center for Devices and Radiological Health oversight, which are not addressed in section 507 of the FD&C Act.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on the ''Qualification Process for Drug Development Tools.'' 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.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). The previously approved collections of information are subject to review by OMB under the PRA. The collections of information pertaining to submissions of investigational new drug applications have been approved under OMB control number 0910–0014; the collections of information pertaining to submissions of new drug applications and abbreviated new drug applications have been approved under OMB control number 0910–0001; and the collections of information pertaining to submissions of biologics license applications in 21 CFR part 601 have been approved under OMB control number 0910–0338.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either *https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics,* or *https://www.regulations.gov.*

Dated: November 19, 2020.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2020–26051 Filed 11–24–20; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2017–D–5739]

Formal Meetings Between the Food and Drug Administration and Abbreviated New Drug Application Applicants of Complex Products Under Generic Drug User Fee Amendments; 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 final guidance for industry entitled ''Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA.'' This guidance describes an enhanced pathway for discussions between FDA and a prospective applicant preparing to submit (or an applicant that has submitted) to FDA an abbreviated new drug application (ANDA) for a complex product. Specifically, this guidance provides information on requesting and conducting product development meetings, presubmission meetings, and midreview cycle meetings with FDA. This guidance will assist applicants in generating and submitting a meeting request and the associated meeting package to FDA for complex products to be submitted under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and as contemplated in the commitments made by FDA in connection with the reauthorization of the Generic Drug User Fee Amendments for Fiscal Years (FYs) 2018–2022 (GDUFA II). This guidance finalizes the draft guidance of the same title issued on October 3, 2017.

DATES: The announcement of the guidance is published in the **Federal Register** on November 25, 2020.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time 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.''