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: Christine Lincoln, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave. Bldg. 22, Rm. 2118, Silver Spring, MD 20993–0002, email: *Christine.Lincoln@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: The use of tumor genetic profiling in cancer treatment decision making has transformed therapeutic strategies in many adult cancers. Extension of this approach to treatment decision making for children with cancer, however, has been greatly diminished due to delays in evaluation of potentially active drugs. Until the passage of section 504 of FDARA, section 505B of the FD&C Act (21 U.S.C. 355c) has not typically been a useful mechanism to require the development of drugs for pediatric cancers, since most of the oncology drugs approved for adults are used to treat cancers that very rarely or never occur in children (*e.g.* cancers of the lung, prostate and breast). Therefore, historically, drug sponsors have requested and obtained waivers for conducting the required assessments of these drugs in pediatric patients. Additionally, drugs developed for rare cancer indications that received orphan designation are exempted from the pre-FDARA requirement to conduct pediatric assessments—even if the cancers those products are intended to treat occur in both adult and pediatric patients—due to the fact that the orphan designation exempts them from such studies (see section 505B(k) of the FD&C Act). However, FDARA amended section 505B so that the requirement for pediatric investigations of drugs directed at molecular targets determined to be substantially relevant to the growth and progression of a pediatric cancer apply even when the adult indication has received an orphan designation, or when the adult indication does not occur, in the pediatric population (*e.g.,* prostate cancer).

Although requirements to study investigational therapies in pediatric oncology were exceedingly rare, other incentives have been put into place to promote the development of oncology products for pediatric cancer. Section 505A of the FD&C Act (21 U.S.C. 355a) provides incentives, in the form of 6 months of additional marketing exclusivity, to encourage sponsors of investigational therapies to conduct pediatric studies of medicines with the potential for use in children. To date, section 505A has been one of the few mechanisms available to incentivize evaluation of new oncology products in children and adolescents. Nevertheless, further development of more novel products that address the substantial unmet needs of the pediatric population is needed.

Section 504 of FDARA requires FDA, with input from the National Cancer Institute (NCI) and others, to develop and regularly update: (1) A list of molecular targets that are determined to be substantially relevant to the growth and progression of a pediatric cancer, and that may trigger the requirement for pediatric investigations under section 505B of the FD&C Act, and (2) a list of molecular targets of new cancer drugs and biological products in development for which the requirement for pediatric investigations under section 505B of the FD&C Act would be automatically waived.

To date, a total of 205 candidate molecular targets were identified from peer-reviewed literature searches, review of publicly available genomic databases, such as NCI Genomic Data Commons, TARGET (Therapeutically Applicable Research to Generate Effective Targets), St. Jude PeCan Data Portal, Ped PanCan, and INFORM (Individualized Therapy for Relapsed Malignancies in Childhood), and input from international subject matter experts. Of these, 62 (30.3 percent) target a gene abnormality, 40 (19.5 percent) target a cell lineage determinant, 21 (10.2 percent) target the tumor microenvironment or the immune system, and 77 (37.6 percent) are classified as ''Others.'' Five (2.4 percent) are candidates for automatic waivers.

Dated: October 11, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–22565 Filed 10–16–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–3138]

Agency Information Collection Activities; Proposed Collection; Comment Request; Experimental Study of an Accelerated Approval Disclosure

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information and to allow 60 days for public comment in response to the notice. This notice solicits comments on research entitled ''Experimental Study of an Accelerated Approval Disclosure.'' This study will examine the presence, wording, and prominence of a disclosure communicating information related to the drug's accelerated approval in direct-to-consumer (DTC) promotional materials.

DATES: Submit either electronic or written comments on the collection of information by December 17, 2018.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before December 17, 2018. The *https://www.regulations.gov* electronic filing system will accept comments until midnight Eastern Time at the end of December 17, 2018. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

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–2018–N–3138 for ''Experimental Study of an Accelerated Approval Disclosure'' 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.gpo.gov/fdsys/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: Ila S. Mizrachi, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–7726, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501–3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. ''Collection of information'' is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Experimental Study of an Accelerated Approval Disclosure

OMB Control Number 0910—NEW

Section 1701(a)(4) of the Public Health Service Act (PHS Act) (42 U.S.C. 300u(a)(4)) authorizes FDA to conduct research relating to health information. Section 1003(d)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(d)(2)(C)) authorizes FDA to conduct research relating to drugs and other FDA-regulated products in carrying out the provisions of the FD&C Act.

The Office of Prescription Drug Promotion's (OPDP) mission is to protect the public health by helping to ensure that prescription drug information is truthful, balanced, and accurately communicated so that patients and health care providers can make informed decisions about treatment options. The OPDP's research program supports this mission by providing scientific evidence to help ensure that our policies related to prescription drug promotion will have the greatest benefit to public health. Toward that end, we have consistently conducted research to evaluate the aspects of prescription drug promotion that we believe are most central to our mission, focusing in particular on three main topic areas: Advertising features, including content and format; target populations; and research quality. Through the evaluation of advertising features we assess how elements such as graphics, format, and disease and product characteristics impact the communication and understanding of prescription drug risks and benefits; focusing on target populations allows us to evaluate how understanding of prescription drug risks and benefits may vary as a function of audience; and our focus on research quality aims at maximizing the quality of research data through analytical methodology development and investigation of sampling and response issues. This study falls under the topic of advertising features (content and format).

Pursuant to section 506(c) of the FD&C Act (21 U.S.C. 356 (c)) and 21 CFR part 314, subpart H (or 21 CFR part 601, subpart E for biological products), FDA may grant accelerated approval to a drug product under section 505(c) (21 U.S.C. 355 (c)) of the FD&C Act or a

biological product under section 351(a) of the PHS Act (42 U.S.C. 262(a)). This pathway enables faster approval of prescription drugs intended to treat serious or life-threatening illnesses. Accelerated approval may be based on a determination that a drug product has an effect on a surrogate endpoint (for example, a blood test result) that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit (*i.e.,* an intermediate clinical endpoint). In approving a drug under the accelerated approval pathway, the severity, rarity, or prevalence of a condition, and the availability or lack of alternative treatments, are taken into account.

The accelerated approval pathway is limited to certain products intended to treat serious or life-threatening illnesses as there can be ''[u]ncertainty about whether clinical benefit will be verified and the possibility of undiscovered risks'' (2014 Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics; available at *https://www.fda.gov/downloads/Drugs/Guidances/UCM358301.pdf*). Sponsors are generally required to conduct post approval studies to verify and describe the predicted clinical benefit, but those confirmatory studies are not complete at the time that the accelerated approval is granted (Ref. 1). In the event that the required post approval confirmatory studies fail to verify and describe the predicted effect or clinical benefit, a drug's approval can be withdrawn using expedited procedures.

Under FDA's regulations governing physician labeling for prescription drugs, the INDICATIONS AND USAGE section of the FDA-approved prescribing information (PI) for a drug approved under accelerated approval must include a succinct description of the limitations of usefulness of the drug and any uncertainty about anticipated clinical benefits, with reference to the clinical studies section for a discussion of the available evidence (21 CFR 201.57(c)(2)(i)(B)). Therefore, the PI for accelerated approval products typically satisfies this requirement by including a statement in the INDICATIONS AND USAGE section about the product's approval under the accelerated approval pathway. In a draft guidance, FDA recommended that the INDICATIONS AND USAGE section for drugs approved under accelerated approval should generally describe three elements: indication(s), limitations of usefulness and clinical benefit uncertainty, and continued approval (Ref. 2). As the PI is intended for healthcare professionals, the information related to a drug's accelerated approval generally includes complex concepts and sophisticated wording. For example, PIs for accelerated approval products include language such as:

- This indication is approved under accelerated approval based on [surrogate endpoint]. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial; or
- Approval is based on a reduction in [surrogate endpoint]. There are no controlled trials demonstrating a direct treatment benefit such as improvement in disease-related symptoms, functioning, or increased survival.

Despite its complexity, sponsors often use this language from the PI in DTC promotional materials for drugs approved under accelerated approval. In other cases, DTC promotion of accelerated approval products does not communicate the unique considerations and potential limitations inherent in the accelerated approval process.

Disclosures may be used to communicate such information to consumers. Disclosures can include information about scientific and clinical data, any residual uncertainty about clinical benefit, and the practical utility of scientific and clinical data. These disclosures may influence consumer comprehension and affect perception of drug's risks and benefits. This study will examine the presence, wording, and prominence of a disclosure communicating information related to the drug's accelerated approval in DTC promotional materials. This information includes the use of surrogate or intermediate clinical endpoints to support approval, the uncertainty about the relationship of the surrogate or intermediate clinical endpoint to the predicted clinical benefit, and the need for confirmatory trials.

We plan to conduct one pretest not longer than 20 minutes, administered via internet panel, to test the experimental manipulations and pilot the main study procedures. After implementing any lessons learned from the pilot, we then plan to conduct one main study not longer than 20 minutes, administered via internet panel. For the pretest and main study, we will randomly assign the voluntary participants to one of the test conditions (see table 1 for the study design). We have chosen to focus on oncology products because cancer is a life-threatening illness, and many oncology products are granted accelerated approval. Moreover, DTC promotion of oncology drugs is common. In the study, participants will view a website for a fictional oncology prescription drug. After viewing the website, participants will complete a questionnaire that assesses whether participants noticed the disclosure and their interpretation of it, as well as perceptions of the drug's risks and benefits. We will also measure covariates such as demographics and literacy. The questionnaire is available upon request from *DTCresearch@fda.hhs.gov.*

We will vary the presence and prominence of the disclosure (*e.g.,* size, color, and location). We hypothesize that participants will be more likely to notice the disclosure when it is presented more, rather than less, prominently. In turn, we expect that participants' perceptions of the drug are more likely to be affected by the disclosure in the high prominence condition. We also will vary whether the disclosure is written in consumer-friendly language or uses language, in use by many sponsors, which is the same as or similar to that directed at healthcare professionals in FDA-approved prescription drug labeling for accelerated approval products. The consumer-friendly version of the accelerated approval disclosure will be based on consumer feedback elicited in focus groups conducted prior to the pretest (approved under OMB control number 0910–0695). The physician labeling version of the accelerated approval disclosure will be drawn from FDA-approved physician labeling. We hypothesize that participants will be more likely to notice and understand the disclosure and use it to form their perceptions of the drug if they view the consumer-friendly language. To test these hypotheses, we will conduct inferential statistical tests such as logistic regression and analysis of variance.

TABLE 1—STUDY DESIGN

	High prominence	Low prominence	Absent
Physician labeling version. Consumer-friendly version.			

We will recruit a general population sample of adult volunteers 18 years of age or older. We will exclude individuals who work for the U.S. Department of Health and Human Services or work in the health care, marketing, advertising, or pharmaceutical industries. We will use health literacy quotas to ensure that our sample includes participants with a range of health literacy skills. With the sample sizes described below, we will have sufficient power to detect small-sized effects in the main study (table 2).

FDA estimates the burden of this collection of information as follows:

TABLE 2—ESTIMATED ANNUAL REPORTING BURDEN [1]

Activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Pretest screener	916	1	1	0.08 (5 min.)	73.28
Study screener	1,507	1	1	0.08 (5 min.)	120.56
Pretest	385	1	1	0.33 (20 min.)	127.05
Main Study	633	1	1	0.33 (20 min.)	208.89
Total					529.78

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

References

The following references are on display at the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20857, and is available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; the reference marked with an asterisk is also available electronically at *https://www.regulations.gov.* The reference without an asterisk is not on public display at *https://www.regulations.gov* because it has copyright restriction, or it is available as a published article. FDA has verified the website address, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

1. Beaver J.A., L.J. Howie, L. Pelosof, et al. ''A 25-Year Experience of U.S. Food and Drug Administration Accelerated Approval of Malignant Hematology and Oncology Drugs and Biologics: A Review.'' *JAMA Oncology.* 2018; 4(6):849–856. doi:10.1001/jamaoncol.2017.5618.

2. FDA Draft Guidance for Industry: Labeling for Human Prescription Drug and Biological Products Approved Under the Accelerated Approval Pathway (March 2014) (*https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM390058.pdf*).

Dated: October 11, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–22570 Filed 10–16–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2017–E–6541]

Determination of Regulatory Review Period for Purposes of Patent Extension; DUPIXENT

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or the Agency) has determined the regulatory review period for DUPIXENT and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Director of the U.S. Patent and Trademark Office (USPTO), Department of Commerce, for the extension of a patent which claims that human biological product.

DATES: Anyone with knowledge that any of the dates as published (see the **SUPPLEMENTARY INFORMATION** section) are incorrect may submit either electronic or written comments and ask for a redetermination by December 17, 2018. Furthermore, any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period by April 15, 2019. See ''Petitions'' in the **SUPPLEMENTARY INFORMATION** section for more information.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before December 17, 2018. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of December 17, 2018. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

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