Withdrawal of approval of an application or abbreviated application under § 314.150(c) is without prejudice to refiling.

Application No.	Drug	Applicant
NDA 009165	Delatestryl (testosterone enanthate) Injection, 200 milligrams (mg)/milliliter (mL).	Endo Pharmaceuticals, Inc., 1400 Atwater Dr., Malvern, PA 19355.
NDA 010417	Xylocaine (lidocaine hydrochloride (HCl)) 4% Topical Solution/Sterile Injection.	Fresenius Kabi, USA, LLC, Three Corporate Dr., Lake Zurich, IL 60047.
NDA 016297	Xylocaine (1.5% lidocaine HCl with dextrose 7.5%) Spinal Injection, 2 mL ampules.	Do.
NDA 016724	Norinyl 1+80 (mestranol and norethindrone) 21-Day Tablets, 0.08 mg/1 mg.	GD Searle LLC, a subsidiary of Pfizer Inc., 235 East 42nd St., New York, NY 10017.
NDA 016725	Norinyl 1+80 (mestranol and norethindrone) 28-Day Tablets, 0.08 mg/1 mg.	Do.
NDA 019217	Sodium Chloride 0.9% Injection USP in Plastic Container, 9 mg/mL.	ICU Medical, Inc., 600 N. Field Dr., Lake Forest, IL 60045.
NDA 019222	Dextrose 5% Injection USP in Plastic Container, 50 mg/mL	Do.
NDA 203098	Testosterone Gel, 2.5 mg/1.25 grams (g), 25 mg/2.5 g, 50 mg/5 g.	Perrigo Co., U.S. Agent for Perrigo Israel Pharmaceuticals Ltd., 3490 Quebec Ave. North, Minneapolis, MN 55427.
NDA 204031	Xartemis XR (oxycodone HCl and acetaminophen) Extended-Release Tablets, 7.5 mg/325 mg.	Mallinckrodt Inc., 675 McDonnell Blvd., Hazelwood, MO 63042.
NDA 205777	Targiniq ER (naloxone HCl and oxycodone HCl) Extended-Release Tablets, 5 mg/10 mg, 10 mg/20 mg, and 20 mg/40 mg.	Purdue Pharma, LP, One Stamford Forum, Stamford, CT 06901–3431.

Therefore, approval of the applications listed in the table, and all amendments and supplements thereto, is hereby withdrawn as of November 28, 2018. Introduction or delivery for introduction into interstate commerce of products without approved new drug applications violates section 301(a) and (d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(a) and (d)). Drug products that are listed in the table that are in inventory on November 28, 2018 may continue to be dispensed until the inventories have been depleted or the drug products have reached their expiration dates or otherwise become violative, whichever occurs first.

Dated: October 23, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–23528 Filed 10–26–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–0821]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Investigation of Consumer Perceptions of Expressed Modified Risk Claims

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by November 28, 2018.

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202–395–7285, or emailed to *oira_submission@omb.eop.gov.* All comments should be identified with the OMB control number 0910–NEW and title ''Investigation of Consumer Perceptions of Expressed Modified Risk Claims.'' Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–8867, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Investigation of Consumer Perceptions of Expressed Modified Risk Claims

OMB Control Number 0910—NEW

I. Background

FDA's Center for Tobacco Products proposes to conduct a study to develop generalizable scientific knowledge to help inform its implementation of section 911 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 387k), wherein FDA will be evaluating information submitted to the Agency about how consumers understand and perceive modified risk tobacco products (MRTPs). Section 911 of the FD&C Act authorizes FDA to grant orders to persons to allow the marketing of MRTPs. The term ''modified risk tobacco product'' means any tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products. FDA can issue a risk modification order under section 911(g)(1) of the FD&C Act authorizing the marketing of an MRTP only if the Agency determines that the product, as it is used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products (section 911(g)(1) of the FD&C Act). Alternatively, with respect to tobacco products that may not be commercially marketed under section 911(g)(1) of the FD&C Act, FDA may issue an exposure modification order under section 911(g)(2) of the FD&C Act authorizing the marketing of an MRTP if the Agency determines that the standard in section 911(g)(2) of the FD&C Act is met, including, among other requirements, that: Any aspect of the label, labeling, or advertising that would cause the product to be an MRTP

is limited to an explicit or implicit representation that the tobacco product or its smoke does not contain or is free of a substance or contains a reduced level of a substance, or presents a reduced exposure to a substance in tobacco smoke; the order would be appropriate to promote the public health; the issuance of the order is expected to benefit the population as a whole, taking into account both users and nonusers of tobacco products; and the existing evidence demonstrates that a measurable and substantial reduction in morbidity and mortality among individual tobacco users is reasonably likely to be shown in subsequent studies (section 911(g)(2) of the FD&C Act). In addition, section 911 of the FD&C Act requires that any advertising or labeling concerning modified risk products enable the public to comprehend the information concerning modified risk and to understand the relative significance of such information in the context of total health and in relation to all the diseases and health-related conditions associated with the use of tobacco products (section 911(h)(1) of the FD&C Act). The proposed research will inform the Agency's efforts to implement the provisions of the FD&C Act related to MRTPs.

FDA proposes conducting a study to assist in determining appropriate methods for gathering information about how consumers perceive and understand modified risk information. The study would develop and validate measures of consumer perceptions of health risk from using tobacco products. Moreover, the study would test how participants' responses on these measures are affected by viewing modified risk labeling or advertising, participants' characteristics such as prior beliefs about the harmfulness of tobacco products, current use of tobacco products, and sociodemographic characteristics. Finally, the study would examine factors that may influence the effectiveness of debriefing at the end of a consumer perception study to ensure that people read and recall key information about the study. This research is significant because it will validate methods that can be used in studies of the impact of labels, labeling, and advertising on consumer perceptions and understanding of the risks of product use.

Measures of consumer health risk perception will be developed and validated by conducting a study on two product types: Moist snuff smokeless tobacco products and electronic cigarette (e-cigarette) products. For each product type, we will assess individual-level factors that may moderate the impact of modified risk information on consumer responses. Potential moderating factors under study include: Beliefs (prior to viewing the modified risk information) about the harmfulness of tobacco products, and the strength with which those beliefs are held; current tobacco use behaviors; and sociodemographic characteristics including age and educational attainment. For each product type, participants will be randomized to view one of two conditions: Tobacco product labeling and advertising that either does or does not contain modified risk claims about a product. The labeling will consist of a product package. The advertising will consist of a print advertisement. The study will assess participants' perceptions of various health risks from using the product, as well as their perceptions of health risk from using the product compared to smoking cigarettes, using nicotine replacement therapies, and quitting all tobacco and nicotine products. The study will also assess participants' intentions to use the product and their level of doubt about whether tobacco products are harmful to users' health. Measures of intentions and doubt will be used to help assess the validity of the measures of health risk perception.

In the **Federal Register** of May 21, 2018 (83 FR 23464), FDA published a 60-day notice requesting public comment on the proposed collection of information. FDA received four comments that were PRA related. Within those submissions, FDA received multiple comments which the Agency has addressed.

(Comment) Three of the comments were supportive of the usefulness and importance of the proposed data collection. These comments stated that validated measures of consumers' health risk perceptions could be useful for FDA, researchers in the field, and industry—in particular, sponsors of modified risk tobacco product applications (MRTPAs). One of these comments expressed hope that the proposed study would be part of a more general effort by FDA to establish methods and standards for evaluating other aspects of MRTPAs.

(Response) FDA agrees with these comments to the extent they relate to this study.

(Comment) One of the comments was unsupportive of the proposed data collection, stating that it should not be undertaken for two reasons. The comment stated that the data are unneeded because U.S. consumers already understand the negative health effects of tobacco use and will not use a tobacco product if they are concerned about their health.

(Response) The proposed data collection focuses on consumer perceptions of modified risk tobacco products, which are products that are sold or distributed for use to reduce harm or the risk of tobacco-related diseases associated with commercially marketed tobacco products.

(Comment) A comment stated that the proposed data collection should not be undertaken because it would waste taxpayers' money.

(Response) FDA believes this study will provide information important to its implementation of The Family Smoking Prevention and Tobacco Control Act. FDA also notes that the study is not funded by taxpayers' money, but rather by industry user fees paid by regulated tobacco companies.

(Comment) One comment suggested that the proposed data collection should be guided by a theoretical approach.

(Response) The main objective of the data collection—developing and validating measures of consumer perceptions of tobacco health risks—is intentionally atheoretical. We intend for this aspect of the research to be data-driven rather than theory-driven. To accomplish this, we have created a large pool of risk perception items by aggregating items from all of the multi-item measures we could find in the published tobacco literature, putting them into the main categories of tobacco health effects that have been identified in prior health reviews, changing the wording of the items to put them in a common format, eliminating redundant or poorly worded items by consulting expert colleagues in medicine, epidemiology, and social science, and adding items to fill remaining gaps in terms of the main categories of tobacco health effects. When analyzing data from this proposed data collection, we plan to use factor analysis to identify the main dimensions underlying how U.S. consumers perceive tobacco product risks. Thus, overall, the goal of the proposed measurement development research is to comprehensively assess risk perceptions without overlaying our own preconceptions about how people may perceive these risks.

(Comment) One comment stated that the findings from our proposed analyses of moderation effects—in particular, the moderating effects of prior beliefs and the certainty with which those beliefs are held—should be considered exploratory, given that these effects are not well established in prior literature. Relatedly, another comment pointed out that the findings from these moderation

analyses may only apply to moist snuff smokeless tobacco and e-cigarette products, given that these are the product types under study in this proposed data collection.

(Response) FDA agrees that the findings of these analyses will be novel in the tobacco literature, and we plan to encourage others to replicate and extend our findings. However, we also note that the measures used in this part of the study were adapted from measures developed and used previously in the attitude certainty literature, and the hypotheses about the potential moderating effects of belief certainty were developed based on prior studies of attitude certainty (Refs. 1 and 2). Thus, there is related literature that will help us interpret our findings on this topic.

(Comment) A comment encouraged FDA to consider how to account for participants' prior beliefs when the tobacco product under study has not been previously marketed in the United States and is therefore unknown to U.S. consumers.

(Response) Our hypothesis would be that consumers may tend to be less certain about their beliefs about such unknown products, and therefore their beliefs about such products may be more susceptible to influence by modified risk information—but this is a hypothesis that has not been empirically tested. We agree that our findings from the proposed analyses of the moderating effects of prior beliefs will benefit from replication and extension by others.

(Comment) One comment suggested that we should consider making four changes to the proposed data collection methodology. First, this comment suggested modifying the study design to change it from a between-subjects design (*i.e.,* in which participants are randomized to conditions and complete a posttest) to a mixed factorial design (*i.e.,* in which participants complete a pretest, are randomized to conditions, and then complete a posttest). The comment stated that this modified design, described as a pretest-posttest-control-group design, would allow us to control for pretest scores, which would ''explicitly minimize the potential threat to internal validity, namely, selection bias.''

(Response) There are advantages and disadvantages to this alternative design type. Whereas the pretest-posttest-control-group design may help determine whether there is anything unusual about the sample that would reduce its representativeness of the target population (*i.e.,* caused by biased selection), using this design would require participants to respond to the key measures twice within a short period of time. This would significantly lengthen the study, which is currently estimated to take approximately 20 minutes, and may influence how participants respond on the posttest (*e.g.,* because of boredom or frustration with repetitive items, testing effects, or demand characteristics). Instead, we propose to use the original, between-subjects design and to conduct analyses to examine the sociodemographic and other characteristics of the sample to understand its representativeness of the U.S. population and to test the success of the randomization procedure.

(Comment) A comment suggested that we should consider using a newly developed measure of participants' intentions to use tobacco products rather than the currently proposed intention items. The comment noted that the currently proposed items are based on prior research but stated that the new measure was developed and validated following procedures in FDA's (2009) guidance on patient-reported outcome measures.

(Response) We appreciate this comment and support the continued development and validation of intention measures. However, at this time, we cannot use this newly developed measure because the research supporting its use has not yet been published in a peer-reviewed journal.

(Comment) A comment suggested that this proposed data collection should assess many more of participants' pre-existing beliefs and attitudes. As examples, the comment suggested assessing participants' skepticism and perceived truthfulness of modified risk claims, stating that this would allow us to more fully capture the key constructs that explain why some people are more likely than others to recall and comprehend the claims.

(Response) As with the recommendations above, we appreciate this suggestion but propose not to assess these additional constructs in this data collection because of concerns about participant burden. The proposed data collection is not intended to comprehensively assess influences on consumer responses to modified risk claims. Rather, it is intended to achieve several specific goals such as developing measures and testing novel potential moderators of the effects of modified risk information. The constructs proposed in this comment have been studied in prior research, as have additional constructs such as brand loyalty (November 19, 2014 (79 FR 68888)). Assessing such constructs may be informative but is not required to achieve the goals of the current proposed data collection.

(Comment) To assist with this project's measurement validation aims, this comment recommended that the study should collect two types of evidence discussed in an FDA guidance on patient-reported outcome measures (FDA, 2009): Evidence of the measures' content validity, such as open-ended input from appropriate populations, and evidence of reliability, other aspects of validity, and sensitivity to detect change.

(Response) The proposed data collection is consistent with both these recommendations. As described above, to achieve content validity, we developed our initial pool of items to be as comprehensive as possible, consulting multi-item measures used previously in the tobacco literature, literature on the objective health effects of tobacco use, and expert colleagues. Additionally, we cognitively tested our pool of items in individual, qualitative interviews with tobacco users and non-users to evaluate their understanding of the items and beliefs about product risks. These interviews included open-ended questions, as recommended. Moreover, the proposed data collection is designed to test the performance of our measures on the criteria discussed in the comment, including internal consistency reliability, other aspects of validity (*e.g.,* known groups, convergent, and discriminant validity), and sensitivity to detect changes (*i.e.,* based on responsiveness to viewing advertisements with vs. without modified risk information). Other performance measures such as test-retest reliability must await further study.

(Comment) Lastly, one comment requested that we clarify how the proposed data collection will assist in measuring consumers' understanding of modified risk information, in addition to their perceptions of health risk.

(Response) In our conceptualization, risk perceptions are a component of consumer understanding, which also includes other components. The goal of the present study is to develop and validate measures of understanding insofar as this construct includes people's perceptions of absolute and relative health risks of using tobacco products.

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

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

Activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Invitation: Young Adults (Ages 18–25)	29,000	1	29,000	0.02 (1 minute)	580
Invitation: Adults (Ages 26+)	29,000	1	29,000	0.02 (1 minute)	580
Consent and Screener: Young Adults (Ages 18–25).	11,000	1	11,000	0.10 (6 minutes)	1,100
Consent and Screener: Adults (Ages 26+)	16,500	1	16,500	0.10 (6 minutes)	1,650
Study: Young Adults (Ages 18–25)	3,300	1	3,300	0.33 (20 minutes)	1,089
Study: Adults (Ages 26+)	3,300	1	3,300	0.33 (20 minutes)	1,089
Total					6,088

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

FDA's burden estimate is based on prior experience with research that is similar to this proposed study. Approximately 58,000 people will receive a study invitation, estimated to take 1 minute to read (approximately 0.02 hour), for a total of 1,160 hours for invitations. Approximately 27,500 people will complete the informed consent and screener to determine eligibility for participation in the study, estimated to take 6 minutes (0.10 hour), for a total of 2,750 hours for informed consent and screening activities. Approximately 6,600 people will complete the full study, estimated to take 20 minutes (approximately 0.33 hour), for a total of 2,178 hours for study completion activities. The estimated total hour burden of the collection of information is 6,088 hours.

II. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at *https://www.regulations.gov.* References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

1. Tormala, Z.L. and D.D. Rucker, ''Attitude Certainty: A Review of Past Findings and Emerging Perspectives.'' *Social and Personality Psychology Compass,* 1:469–492, 2007. doi:10.1111/j.1751–9004.2007.00025.x.

2. Tormala, Z.L. and D.D. Rucker, ''Attitude Certainty: Antecedents, Consequences, and New Directions.'' *Consumer Psychology Review,* 1:72–89, 2018. doi:10.1002/arcp.1004.*

Dated: October 23, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–23523 Filed 10–26–18; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–1726]

Circulatory System Devices Panel of the Medical Devices Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) announces a forthcoming public advisory committee meeting of the Circulatory System Devices Panel of the Medical Devices Advisory Committee. The general function of the committee is to provide advice and recommendations to the Agency on FDA's regulatory issues. The meeting will be open to the public.

DATES: The meeting will be held on December 4 and 5, 2018, from 8 a.m. to 6 p.m.

ADDRESSES: Hilton Washington DC North/Gaithersburg, Salons A, B, C, and D, 620 Perry Pkwy., Gaithersburg, MD 20877. The hotel telephone number is 301–977–8900; additional information available online at: *https://www3.hilton.com/en/hotels/maryland/hilton-washington-dc-north-gaithersburg-GAIGHHF/index.html.* Answers to commonly asked questions including information regarding special accommodations due to a disability, visitor parking, and transportation may be accessed at: *https://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/ucm408555.htm.*

FOR FURTHER INFORMATION CONTACT: Patricio Garcia, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. G610, Silver Spring, MD 20993–0002, *patricio.garcia@fda.hhs.gov,* 301–796–6875, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area). A notice in the **Federal Register** about last minute modifications that impact a previously announced advisory committee meeting cannot always be published quickly enough to provide timely notice. Therefore, you should always check the Agency's website at *https://www.fda.gov/AdvisoryCommittees/default.htm* and scroll down to the appropriate advisory committee meeting link, or call the advisory committee information line to learn about possible modifications before coming to the meeting.

SUPPLEMENTARY INFORMATION:

Agenda: On December 4, 2018, the committee will discuss, make recommendations, and vote on information regarding the premarket application (PMA) for the OPTIMIZER SMART Implantable Pulse Generator device, sponsored by Impulse Dynamics (USA), Inc. This first-of-a-kind device is indicated to provide cardiac contractility modulation for class III heart failure patients who are not responding to optimal medical therapy.

On December 5, 2018, the committee will discuss and make recommendations regarding issues relating to the emergence of medical devices, which aim to treat hypertension. Currently, clinical studies to evaluate the safety and effectiveness of these devices are progressing. FDA requests panel input regarding the potential indications and labeling for devices intended to treat hypertension and optimal study designs needed to