opioid antagonist with high affinity for the mu opioid receptor. The naloxone is intended to be inactive when SUBOXONE is used appropriately, but to precipitate more severe withdrawal symptoms if the product is crushed and injected by an individual dependent on full opioid agonists. A variety of factors such as degree of opioid dependence, relative amount of buprenorphine exposure, and route of administration influence the antagonist effect of naloxone. As a result, buprenorphine/naloxone combination products may not have the same effect on non-dependent opioid abusers or abusers of buprenorphine. As stated in the approved SUBOXONE labeling in section 12.2, ''naloxone in buprenorphine/naloxone tablets may deter injection of buprenorphine/naloxone tablets by persons with active substantial heroin or other full mu-opioid dependence,'' but ''some opioid-dependent persons, particularly those with a low level of full mu-opioid physical dependence or those whose opioid physical dependence is predominantly to buprenorphine, abuse buprenorphine/naloxone combinations by the intravenous or intranasal route.''

SUBUTEX has important therapeutic benefits for certain patient populations that may not tolerate or should not be exposed to the naloxone in SUBOXONE. Specifically, as explained in section 5.11 of the approved labeling for SUBOXONE, ''[b]uprenorphine/naloxone products are not recommended in patients with severe hepatic [liver] impairment and may not be appropriate for patients with moderate hepatic impairment.'' Section 5.11 further states that ''hepatic impairment results in a reduced clearance of naloxone to a much greater extent than buprenorphine,'' and thus, ''patients with severe hepatic impairment will be exposed to substantially higher levels of naloxone than patients with normal hepatic function.'' SUBUTEX also is preferred to SUBOXONE for patients transitioning from treatment with methadone or other long-acting opioid products because they are at higher risk for precipitated and prolonged withdrawal, and the naloxone in buprenorphine/naloxone combination products may cause worse withdrawal in this population.

Although Reckitt has publicly stated that SUBUTEX ''creates a greater risk of misuse, abuse, and diversion'' than SUBOXONE (please refer to letter from Reckitt to Health Care Providers, available at *http://buprenorphine.samhsa.gov/SubutexDiscontinuation9-16-11.pdf*), Reckitt has not submitted any data, information, or analysis to support this claim. Based on our independent review of the available data and the published studies on the relative abuse liability of SUBUTEX and SUBOXONE, we do not have sufficient information at this time to determine that SUBUTEX poses an increased potential for abuse or misuse relative to SUBOXONE. Furthermore, as discussed previously, SUBUTEX has important therapeutic benefits for certain patient populations that may not tolerate or should not be exposed to the naloxone in SUBOXONE.

For these reasons, based on the data and information available to the Agency at this time, we find that the benefits of SUBUTEX continue to outweigh the risks. Therefore, we conclude that SUBUTEX was not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list SUBUTEX in the ''Discontinued Drug Product List'' section of the Orange Book. The ''Discontinued Drug Product List'' delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. FDA will not begin procedures to withdraw approval of ANDAs that refer to SUBUTEX. Such ANDAs may continue to be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs.

Dated: February 9, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–03001 Filed 2–12–15; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–N–2187]

Identifying Potential Biomarkers for Qualification and Describing Contexts of Use To Address Areas Important to Drug Development; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is seeking information to facilitate development and qualification of biomarkers in areas related to human drug therapeutics. Towards this goal, FDA is encouraging interested groups and individuals to submit information on specific medical and biological areas where novel biomarkers can be identified that would meaningfully advance drug development. FDA encourages respondents to describe evidentiary considerations that are important to qualify these biomarkers for a specific context of use. Details of information that should be provided to the Agency are described in the survey.

DATES: Submit either electronic or written comments by April 14, 2015.

ADDRESSES: You may submit comments by any of the following methods:

Electronic Submissions

Submit electronic comments in either of the following ways:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments.
- *SurveyMonkey Link: https://www.surveymonkey.com/s/RHJLHS7.* This survey may be used to provide feedback on answers to questions regarding potential biomarkers for qualification and to describe contexts of use to address areas important to drug development.

Written Submissions

Submit written submissions in the following ways:

- *Mail/Hand delivery/Courier (for paper submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Docket No. FDA–2014–N–2187 for this document. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided. It is only necessary to send one set of comments. For additional information on submitting comments, see the ''Request for Information'' heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to *http://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 Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Marianne Noone, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 21, Rm. 4528, Silver Spring, MD 20993–0002, 301–796–7495.

SUPPLEMENTARY INFORMATION:

I. Background

The President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144) on July 9, 2012. Title I of FDASIA reauthorizes the Prescription Drug User Fee Act (PDUFA) and provides FDA with the user fee resources necessary to maintain an efficient review process for human drug and biological products. The reauthorization of PDUFA added performance goals and procedures for the Agency that represent FDA's commitments during fiscal years 2013 through 2017. These commitments are fully described in the document entitled ''PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017'' (PDUFA Goals Letter), available on FDA's Web site at *http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf.* Section IX of the PDUFA Goals Letter entitled ''Enhancing Regulatory Science and Expediting Drug Development'' references support for the identification and advancement of biomarkers.

A biomarker is an objective characteristic that is measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to treatment. Biomarkers can serve many purposes in clinical drug development, including the following: Defining the appropriate patient populations for study, as well as those who should receive the drug in clinical practice; pharmacodynamic markers for proof of concept and dose selection; and pharmacodynamic markers of adverse effects. A subset of pharmacodynamic biomarkers can serve as replacements for clinical efficacy endpoints that reflect how a patient feels, functions, or survives. The path to development of promising therapeutics can be enabled by the availability of biomarkers that are analytically validated and clinically qualified for a specific context of use (*i.e.,* a comprehensive, clear, and precise statement that describes the manner of use, interpretation, and purpose of use of a biomarker in drug development).

Qualification is based on a body of evidence that demonstrates that the biomarkers are fit for purpose in drug development and evaluation (*http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284076.htm*). Further, qualification is dependent on the specific proposed context of use. Biomarkers that are qualified can help to progressively reduce uncertainty about the outcome of clinical development programs.

Public/private partnerships involving regulatory, academic, and industry scientists, collaborating within a precompetitive framework, are essential to catalyzing progress. Because of limitations in resources, such efforts must be focused on the opportunities that offer the greatest potential for impact.

FDA intends to facilitate identification of the most promising biomarkers and the areas important to drug development and to promote efforts that will aid in the qualification and regulatory adoption of the drug development framework.

II. Request for Information

FDA is seeking public feedback to identify promising biomarker candidates in areas important to drug development and to identify considerations for evidence needed to qualify various types of biomarkers for specific contexts of use. FDA requests identification of specific biomarkers with a proposed context of use and of the type of evidence needed to support qualification. After reviewing the information provided, FDA will post the collated information on its Web site.

A. Information Requirements

In general, submitted information should include the following for each biomarker nominated, as well as any other relevant information:

- Areas that have a critical need for biomarkers to assist drug development;
- The name of the biomarker;
- The proposed context of use for the biomarker (if known);
- The reason why the biomarker should be considered, taking into account its usefulness as a drug development tool; and
- Any evidence that should be developed to support qualification of the biomarker.

B. Questions and Requests

Specific questions and requests are as follows:

1. Are there specific aspects of drug development that could be enhanced through the development of biomarkers?

a. Please list the specific applications of biomarkers that address areas important to drug development.

b. Please list the specific areas (for example, a specific disease area or an organ toxicity) needed for development of biomarkers important to drug development.

c. Is there information or efforts which could be leveraged to advance these areas? If yes, please describe.

d. Are there areas that appear to be promising for the development of new biomarkers and for which collaborative engagement from stakeholders offers a path forward? If so, please explain.

- Are there groups positioned to accomplish this? If yes, please describe.

e. Are there barriers that preclude engagement or investment in biomarkers for these priority areas? If yes, please explain.

2. In each of these priority areas that are important to drug development, please provide the following information:

a. Biomarker: What specific biomarkers do you believe represent the greatest near-term opportunity to establish utility in drug development (*i.e.,* that could be substantially advanced by facilitating discussion and consensus building)?

b. Rationale: Why should the biomarker(s) be included on the list, taking into account its usefulness in regulatory decisionmaking as a drug development tool?

c. Context of use: Can you please describe/propose a specific context of use for the biomarker(s)?

d. Evidentiary gaps: To support the proposed context of use, what do you see as the largest evidentiary gaps that need to be addressed to permit ''fit for purpose'' qualification?

e. How can these evidentiary gaps be addressed?

f. Collaborative data sharing: Can any of these gaps be addressed by collaborative data sharing of existing data versus prospective studies specifically dedicated to addressing the gap?

3. Please indicate your affiliation from the following list: Academia, pharmaceutical sector, biotechnology sector, government, professional organization, non-profit organization, clinician, patient advocacy group, patient, or other (please provide specifics, if you choose other).

III. Paperwork Reduction Act

This **Federal Register** notice requests input from biomarker experts from academia, the pharmaceutical industry, and government organizations on the evidentiary standards for biomarkers or on the expectations about data for qualification of different types of biomarkers.

This request is exempt from the Office of Management and Budget's review under 5 CFR 1320.3(h)(4): Facts or opinions submitted in response to general solicitations of comments from the public, published in the **Federal Register** or other publications, regardless of the form or format thereof,

provided that no person is required to supply specific information pertaining to the commenter, other than that necessary for self-identification, as a condition of the Agency's full consideration of the comment.

Dated: February 5, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–02976 Filed 2–12–15; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–N–1049]

Conditional Approval of New Animal Drugs; Public Meeting; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of public meeting; request for comments.

The Food and Drug Administration (FDA) is announcing a public meeting to explore the use of statutory changes to expand the use of conditional approval to additional categories of new animal drugs. This policy exploration is consistent with a stated performance goal in the Animal Drug User Fee Amendments of 2013 (ADUFA III) goals letter. FDA is requesting that you submit any comments related to this issue by September 30, 2015.

Date and Time: The public meeting will be held on March 16, 2015, from 1 p.m. until 4 p.m.

Location: The public meeting will be held at the Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., 3rd Floor, Rockville, MD 20855. Parking is free.

Contact Person: Laura Bradbard, Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rm. 159, Rockville, MD 20855, 240–276–9109, FAX: 240–276–9020, email: *Laura.Bradbard@fda.hhs.gov.*

Registration: Registration is free and available on a first-come, first-served basis. Persons interested in attending this meeting must register by March 10, 2015. For general questions about the meeting, for assistance to register for the meeting, to request an opportunity to make an oral presentation, or to request special accommodations due to a disability, contact Laura Bradbard (see *Contact Person*). Please include your name, organization, and contact information. If you are requesting an opportunity to speak, please send a brief summary of your comments. Early registration for the meeting is encouraged due to limited time and space.

SUPPLEMENTARY INFORMATION:

I. Background

FDA considers the timely review of the safety and effectiveness of new animal drugs to be central to the Agency's mission to protect and promote the public health. Before 2004, the timeliness and predictability of the new animal drug review program was a concern. The Animal Drug User Fee Act enacted in 2003 (Pub. L. 108–130; hereinafter referred to as ''ADUFA I''), authorized FDA to collect user fees for 5 years—fiscal year (FY) 2004 to FY 2008—that were to be dedicated to expediting the review of new animal drug applications according to certain performance goals and to expand and modernize the new animal drug review program. The Agency agreed to meet a comprehensive set of performance goals established to show significant improvement in the timeliness and predictability of the new animal drug review process. The implementation of ADUFA I provided a significant funding increase that enabled FDA to increase the number of staff dedicated to the new animal drug application review process.

In 2008, before ADUFA I expired, Congress passed the Animal Drug User Fee Amendments of 2008 (Pub. L. 110–316; hereinafter referred to as ''ADUFA II''), which included an extension of ADUFA for an additional 5 years—FY 2009 to FY 2013. ADUFA II performance goals were established based on ADUFA I FY 2008 review timeframes. In addition, FDA provided program enhancements to reduce review cycles and improve communications during reviews.

In 2013, before ADUFA II expired, Congress passed ADUFA III (Pub. L. 113–14), which was signed by the President on June 13, 2013. Like its predecessors, ADUFA III includes its own comprehensive set of performance goals. One such goal, as stated in the ADUFA III goals letter, is: Beginning in early FY 2014, the Agency agrees to explore, in concert with industry, the feasibility of pursuing statutory revisions, consistent with the Agency's mission to protect and promote the public health, that may expand the use of conditional approvals to other appropriate categories of new animal drug applications and develop recommendations by September 30, 2015.

Currently, the conditional approval provisions allow an applicant to market a new animal drug intended for a minor species or a minor use in a major species after the applicant has demonstrated that the drug is safe and can be manufactured according to standards applicable to approval of applications under section 512(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(b)(1)). FDA and members of regulated industry jointly agreed to explore, as part of the performance goals outlined in the ADUFA III goals letter, statutory changes to expand the use of conditional approval to other appropriate categories of new animal drugs.

This public meeting is intended to provide an additional opportunity for public comment. The Agency is especially interested in receiving comments during the meeting on the categories of new animal drug applications that would be considered ''appropriate'' and why; concerns, if any, that might arise due to the expansion of the Conditional Approval process; and the length of marketing exclusivity, if any, that should be associated with the expansion of the Conditional Approval process.

FDA will consider comments received at this meeting as it moves forward with this process.

FDA has already opened public docket FDA Docket No. FDA–2014–N–1049 to receive comments on the issue (79 FR 53430, September 9, 2014). Although you can comment on this document at any time, to ensure that the Agency considers your comment before finalizing work on the exploration process described in this document, submit either electronic or written comments by September 30, 2015.

II. Participation in a Public Meeting

While oral presentations from specific individuals and organizations may be limited due to time constraints during the public meeting, stakeholders may submit electronic or written comments discussing any issues of concern to the administration record (the docket). All relevant data and documentation should be submitted with the comments to Docket No. FDA–2014–N–1049. Submit electronic comments to *http://www.regulations.gov.* Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. It is only necessary to send one set of comments. Identify comments with the docket number FDA–2014–N–1049. Received comments may be seen in the Division