TABLE 2—ESTIMATED ANNUAL REPORTING BURDEN [1]

FDA center	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Center for Biologics Evaluation and Research	2,114	1	2,114	1	2,114
Center for Devices and Radiological Health	10,528	1	10,528	2	21,056
Center for Veterinary Medicine	1,848	1	1,848	1	1,848
Total					25,018

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

Dated: February 9, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–03005 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–2013–P–1055]

Determination That SUBUTEX (Buprenorphine Hydrochloride) Sublingual Tablets, Equivalent 2 Milligrams Base and Equivalent 8 Milligrams Base, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that SUBUTEX (buprenorphine hydrochloride (HCl)) Sublingual Tablets, Equivalent (Eq) 2 milligrams (mg) base and Eq 8 mg base, were not withdrawn from sale for reasons of safety or effectiveness. This determination means that FDA will not begin procedures to withdraw approval of abbreviated new drug applications (ANDAs) that refer to SUBUTEX, and it will allow FDA to continue to approve ANDAs that refer to SUBUTEX as long as they meet relevant legal and regulatory requirements.

FOR FURTHER INFORMATION CONTACT: Ayako Sato, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6228, Silver Spring, MD 20993–0002, 240–402–4191.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98–417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA sponsors must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the ''listed drug,'' which is a version of the drug that was previously approved. Sponsors of ANDAs do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the ''Approved Drug Products with Therapeutic Equivalence Evaluations,'' which is known generally as the ''Orange Book.'' Under FDA regulations, a drug is removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

Under § 314.161(a) (21 CFR 314.161(a)), the Agency must determine whether a listed drug was withdrawn from sale for reasons of safety or effectiveness: (1) Before an ANDA that refers to that listed drug may be approved, (2) whenever a listed drug is voluntarily withdrawn from sale and ANDAs that refer to the listed drug have been approved, and (3) when a person petitions for such a determination under 21 CFR 10.25(a) and 10.30.

SUBUTEX (buprenorphine HCl) Sublingual Tablets is the subject of NDA 20–732, held by Reckitt Benckiser Pharmaceuticals, Inc. (Reckitt). It was approved on October 8, 2002. After Reckitt discontinued marketing SUBUTEX in 2011, FDA moved SUBUTEX to the ''Discontinued Drug Product List'' section of the Orange Book. Another buprenorphine-containing product, SUBOXONE (buprenorphine HCl and naloxone HCl) Sublingual Tablets, is the subject of NDA 20–733, also held by Reckitt. It was originally approved on October 8, 2002, and later approved in another dosage form (sublingual film) on August 30, 2010, under NDA 22–410. In March 2013, Reckitt discontinued marketing the sublingual tablet dosage form of SUBOXONE.[1] All three products are approved for treatment of opioid dependence.[2]

Actavis Elizabeth LLC submitted a citizen petition dated August 16, 2013 (Docket No. FDA–2013–P–1055), under 21 CFR 10.30, requesting that FDA determine whether SUBUTEX was withdrawn from sale for reasons of safety or effectiveness. The petition contains no data or other information suggesting that SUBUTEX was withdrawn for reasons of safety or effectiveness.

We have carefully reviewed our records concerning the withdrawal of SUBUTEX from sale. Based on the information we have at this time, FDA has determined under § 314.161 that SUBUTEX was not withdrawn for reasons of safety or effectiveness.

The buprenorphine in both SUBUTEX and SUBOXONE is a mu opioid partial agonist that can precipitate withdrawal in patients physically dependent on full opioid agonists. That is, the relative reduction in activity at the mu receptor when buprenorphine replaces a full opioid agonist can cause symptoms of opioid withdrawal. SUBOXONE also contains naloxone. Naloxone is a potent

[1] On September 27, 2012, after Reckitt publicly announced that it was planning to discontinue the product, Lachman Consultant Services Inc. (Lachman) submitted a citizen petition requesting that the Agency determine whether SUBOXONE Sublingual Tablets were withdrawn from sale for reasons of safety or effectiveness (Docket No. FDA–2012–P–1034). After considering Lachman's citizen petition and reviewing our records, including the analysis that the Agency prepared in connection with Reckitt's citizen petition (Docket No. FDA–2012–P–1028), FDA determined that SUBOXONE Sublingual Tablets was not discontinued for reasons of safety or effectiveness (78 FR 34108).

[2] On September 25, 2012, Reckitt submitted a citizen petition requesting that FDA not approve any new drug application or abbreviated new drug application (ANDA) for a buprenorphine product for treatment of opioid dependence unless the applications and products met certain criteria. On February 22, 2013, FDA denied Reckitt's petition (Docket No. FDA–2012–P–1028).

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]

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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.