information concerning the definition of complete response.

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 BCG-unresponsive nonmuscle invasive bladder cancer. 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. This guidance is not subject to Executive Order 12866.

II. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR parts 312 and 314 have been approved under OMB control numbers 0910–0014 and 0910–0001, respectively.

III. Electronic Access

Persons with access to the internet may obtain the guidance at either https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, https://www.fda.gov/BiologicsBloodVaccines/Guidances/default.htm, https://www.regulations.gov or 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/
were insufficient data showing the solution suitable for injection; (2) there
commonly available solvents into a formulation can be readily extracted in
particular, (1) the oxycodone in the properties, for multiple reasons. In
labeling describing abuse-deterrent is not approvable with the proposed
approved in its present form, describing those properties.

were insufficient to show the product was meaningfully resistant to
manipulation for misuse or abuse; and (4) there were not data submitted,
including data from pharmacokinetic and human abuse liability studies, fully
characterizing the product’s abuse potential by all relevant routes of abuse.
Also, the data submitted were not sufficient to rule out the possibility that
the proposed formulation could result in a greater proportion of abuse by
injection of PMRS’s product compared to a conventional IR oxycodone
formulation. Abuse by injection carries greater risk of overdose and
transmission of infectious disease than abuse by other routes.

The safety and purity of the excipients intended (but not shown) to
confer abuse deterrent properties were not adequately characterized, either by
the intended oral route of use or by expected routes of abuse, including injection.

An overall evaluation of elemental impurities in the final formulation and
a risk assessment for each heavy metal (taking into consideration the maximum
daily dose) were not provided.

The application did not fully comply with the patent certification
requirements applicable to applications submitted under section 505(b)(2)
of the FD&C Act (proposing to rely in part on the Agency’s previous finding of safety and
effectiveness for ROXICODONE (oxycodone HCl) IR Tablets (NDA 021011). PMRS proposed that its oxycodone HCl IR capsules be indicated for the management of acute pain severe
enough to require an opioid analgesic and for which alternative treatments are
inadequate. PMRS also attempted to show that the product had certain abuse-deterrent properties and sought FDA approval of labeling describing
those properties.

On November 16, 2017, the Division of Anesthesia, Analgesia, and Addiction Products of FDA’s Center for Drug Evaluation and Research (CDER) issued a
complete response letter to PMRS under § 314.110(a) (21 CFR 314.110(a)) stating that NDA 209155 could not be approved in its present form, describing the specific deficiencies, and, where possible, recommending ways PMRS
might remedy these deficiencies. The deficiencies include the following:

1. The application in its present form is not approvable with the proposed
labeling describing abuse-deterrent properties, for multiple reasons. In
particular, (1) the oxycodone in the formulation can be readily extracted in
commonly available solvents into a solution suitable for injection; (2) there
were insufficient data showing the presence of excipients (including dye)
in the formulation can be expected to deter abuse by injection; (3) the data
submitted were insufficient to show the proposed formulation would
result in a greater proportion of abuse by injection of PMRS’s product compared to
a conventional IR oxycodone formulation. Abuse by injection carries
greater risk of overdose and transmission of infectious disease than abuse by other routes.

2. The safety and purity of the excipients intended (but not shown) to
confer abuse deterrent properties were not adequately characterized, either by
the intended oral route of use or by expected routes of abuse, including injection.

3. An overall evaluation of elemental impurities in the final formulation and
a risk assessment for each heavy metal (taking into consideration the maximum
daily dose) were not provided.

4. The application did not fully comply with the patent certification
requirements applicable to applications submitted under section 505(b)(2) of the
FD&C Act.

5. The complete response letter describes additional deficiencies, which
generally relate to chemistry, manufacturing, and controls and current
good manufacturing practice requirements, that CDER determined
preclude approval of the application in its present form. The complete response
letter also noted that satisfactory resolution of objectionable inspection
observations was required before the application could be approved. Due to
applicable limitations on public disclosure of information contained in
unapproved NDAs, including trade secret information, these specific
deficiencies are not described in this notice.

The complete response letter stated that PMRS is required to resubmit the
application, fully addressing all deficiencies listed in the letter, or take
other actions available under § 314.110 (i.e., withdraw the application or
request an opportunity for a hearing). Applicable regulations, including
§ 10.75 (21 CFR 10.75), also provide a mechanism for applicants to obtain
formal review of one or more decisions reflected in a complete response letter
(see FDA’s guidance for industry “Formal Dispute Resolution: Sponsor
Appeals Above the Division Level” (November 2017) available at: https://www.fda.gov/downloads/drugs/guidancecomplianceregulatory
information/guidances/ucm343101.pdf).

In response to the complete response letter, on November 17, 2017, PMRS
submitted a request for an opportunity for a hearing under § 314.110(b)(3) on
whether there are grounds under section 505(d) of the FD&C Act for denying
approval of NDA 209155.

II. Notice of Opportunity for a Hearing

For the reasons stated previously and others described in the complete
response letter, notice is given to PMRS and to all other interested persons that
the Center Director proposes to issue an order refusing to approve NDA 209155
on the grounds that the application fails to meet the criteria for approval under
section 505(d) of the FD&C Act, including that: (1) PMRS has not
provided sufficient data to show that the product would be safe (505(d)(1)); (2)
PMRS has not shown that the methods used in, and the facilities and controls
used for the manufacture, processing, or packing of the product are adequate to
preserve its identity, strength, quality, and purity (505(d)(3)); and (3) the
labeling PMRS proposed for the product is false or misleading (505(d)(7)).

PMRS may request a hearing before the Commissioner of Food and Drugs
(the Commissioner) on the Center Director’s proposal to refuse to approve
NDA 209155. If PMRS decides to seek a hearing, it must file: (1) A written
notice of participation and request for a hearing (see the DATES section), and (2)
the studies, data, information, and analyses relied upon to justify a hearing
(see the DATES section), as specified in § 314.200.

As stated in § 314.200(g), a request for a hearing may not rest upon mere
allegations or denials, but must present specific facts showing that there is a
genuine and substantial issue of fact that requires a hearing to resolve. We
note in this regard that because CDER proposes to refuse to approve NDA
209155 for multiple reasons, any hearing request from PMRS must
address all of those reasons, including reasons described in the complete
response letter but not described in this notice due to applicable limitations on
public disclosure of information contained in unapproved NDAs, including trade
secret information. Failure to request a hearing within the time
provided and in the manner
required by § 314.200 constitutes a
waiver of the opportunity to request a
hearing. If a hearing request is
not properly submitted, FDA will issue a
notice refusing to approve NDA 209155.
The Commissioner will grant a hearing if there exists a genuine and substantial issue of fact or if the Commissioner concludes that a hearing would otherwise be of public interest (§ 314.200(g)(6)). If a hearing is granted, it will be conducted according to the procedures provided in 21 CFR parts 10 through 16 (21 CFR 314.201).

Paper submissions under this notice of opportunity for a hearing must be filed in two copies. Except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, submissions may be seen in the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, and on the internet at https://www.regulations.gov. This notice is issued under section 505(c)(1)(B) of the FD&C Act, §§ 314.110(b)(3) and 314.200.

Dated: February 8, 2018.

Janet Woodcock,
Director, Center for Drug Evaluation and Research.

[FR Doc. 2018–02903 Filed 2–12–18; 8:45 am]
BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration


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

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 FARYDAK and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of applications 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 drug product.

DATES: Anyone with knowledge that any of the dates as published (in the SUPPLEMENTARY INFORMATION section) are incorrect may submit either electronic or written comments and ask for a redetermination by April 16, 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 August 13, 2018. 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 April 16, 2018. The https://www.regulations.gov electronic filing system will accept comments until midnight Eastern Time at the end of April 16, 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 Nos. FDA–2015–E–2666; FDA–2015–E–2758; and FDA–2015–E–2664 for “Determination of Regulatory Review Period for Purposes of Patent Extension; FARYDAK.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the dockets 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 § 10.20 (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:
Beverly Friedman, Office of Regulatory Policy, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6250, Silver Spring, MD 20993, 301–796–3600.

SUPPLEMENTARY INFORMATION: