DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–D–3759]

Considerations for the Development of Dried Plasma Products Intended for Transfusion; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft document entitled ''Considerations for the Development of Dried Plasma Products Intended for Transfusion; Draft Guidance for Industry.'' This guidance is intended to assist manufacturers, sponsors, and applicants developing dried plasma products intended for transfusion in order to facilitate the availability of safe and effective dried plasma products in the United States. The draft guidance document provides considerations for the successful development and licensing of dried plasma products and for the approval of devices used to manufacture dried plasma. The guidance includes recommendations on optimal sources of input plasma; manufacturing and product quality, including product characterization; packaging and reconstitution; clinical studies; and device submissions.

DATES: Submit either electronic or written comments on the draft guidance by January 28, 2019 to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

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–D–3759 for ''Considerations for the Development of Dried Plasma Intended for Transfusion; Draft Guidance for Industry.'' Received comments 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.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist the office in processing your requests. The draft guidance may also be obtained by mail by calling CBER at 1–800–835–4709 or 240–402–8010. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Jonathan McKnight, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft document entitled ''Considerations for the Development of Dried Plasma Products Intended for Transfusion; Draft Guidance for Industry.'' Plasma is a critical component of early transfusion therapy in the management of traumatic hemorrhage. Plasma can replenish various coagulation proteins that are consumed during the coagulopathy that can accompany traumatic injury. Because plasma products intended for transfusion such as fresh frozen plasma (FFP), plasma frozen within 24 hours after phlebotomy (PF24), and plasma frozen within 24 hours after phlebotomy held at room temperature up to 24 hours after phlebotomy (PF24, RT24) are stored frozen, these products need to be thawed prior to transfusion. This limits

or prevents the use of plasma in settings where freezers and other support equipment are unavailable (*e.g.* battlefields, remote locations, and other austere settings) and may lead to delayed administration. Dried plasma (such as freeze-dried or spray-dried plasma) offers the potential to address these challenges by providing a product that is stable at ambient temperatures and can be rapidly reconstituted and transfused.

Recent clinical studies have demonstrated promising efficacy and safety of dried plasma, particularly in military applications, and dried plasma products are available for limited use in Germany, South Africa, and France. This guidance is intended to assist manufacturers, sponsors, and applicants developing dried plasma products intended for transfusion in order to facilitate the availability of safe and effective dried plasma products in the United States.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on considerations for the development of dried plasma products intended for transfusion. 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. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information 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 part 211 have been approved under OMB control number 0910–0139; the collections of information in 21 CFR part 312 have been approved under OMB control number 0910–0014; the collections of information in 21 CFR part 601 have been approved under OMB control number 0910–0338; the collections of information in 21 CFR part 610 have been approved under OMB control numbers 0910–0116, 0910–0139, and 0910–0338; the collections of information in 21 CFR part 630 have been approved under OMB control number 0910–0116; the collections of information in 21 CFR part 640 have been approved under OMB control number 0910–0116; the collections of information in 21 CFR part 812 have been approved under OMB control number 0910–0078; and the collections of information in 21 CFR part 814 have been approved under OMB control number 0910–0231.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either *https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm* or *https://www.regulations.gov.*

Dated: October 25, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–23637 Filed 10–29–18; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–0188]

Denial of Hearing Request Regarding Proposal To Refuse To Approve a New Drug Application for Oxycodone Hydrochloride Immediate-Release Abuse-Deterrent Formulation, Oral Capsules, 5 Milligrams, 15 Milligrams, and 30 Milligrams; Order Refusing Approval

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Chief Scientist is denying a request for a hearing regarding the proposal by the Center for Drug Evaluation and Research (CDER) of the Food and Drug Administration (FDA or Agency) to refuse to approve a new drug application submitted by Pharmaceutical Manufacturing Research Services, Inc. (PMRS) for oxycodone hydrochloride (HCl) immediate-release (IR) capsules, 5 milligrams (mg), 15 mg, and 30 mg in its present form. The Chief Scientist denies approval.

DATES: The order is applicable October 30, 2018.

FOR FURTHER INFORMATION CONTACT: Nathan R. Sabel, Office of Scientific Integrity, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, Rm. 4206, Silver Spring, MD 20993, 301–796–8588.

SUPPLEMENTARY INFORMATION:

I. Procedural Background

PMRS submitted new drug application (NDA) 209155 for oxycodone HCl IR capsules, 5 mg, 15 mg, and 30 mg, under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(b)(2)), relying in part on the Agency's previous findings of safety and effectiveness for ROXICODONE (oxycodone HCl IR tablets (NDA 021011)) (Ref. 1).

PMRS's product contains excipients, including a dye blend, that have solubility in common solvents, including water and ethanol, similar to the solubility of the active pharmaceutical ingredient (API). PMRS contends that a solution prepared from its product for subcutaneous or intravenous injection will look relatively ''impure'' compared to a solution prepared from Roxicodone and will have a dark, opaque, ''contaminated-looking'' appearance, providing both a ''visual deterrent'' and a ''chemical deterrent'' to abuse by injection (Refs. 2 and 3).[1] PMRS provided in vitro data intended to show that a solution prepared for injection would have these qualities but provided no data or literature supporting the conclusion that people who inject opioids would, in fact, be deterred from injecting such a solution (Ref. 2).

PMRS also provided in vitro data intended to demonstrate that its product would be more difficult to grind into particle sizes suitable for snorting compared to ROXICODONE but provided no data from studies in human subjects to evaluate the pharmacokinetic or pharmacodynamic properties of the product following abuse via the nasal route (Ref. 1).[2] Nonetheless, PMRS proposed labeling for its product representing that it has abuse-deterrent properties (Ref. 4).

On November 16, 2017, CDER issued a complete response letter to PMRS under § 314.110(a) (21 CFR 314.110(a)) stating that the NDA could not be

[1] With respect to the purported ''chemical deterrent'' aspect of its product, we note that PMRS's claims that its product resists physical and chemical ''extraction'' appear to rest on a misunderstanding of how that term is used in the context of abuse-deterrent opioids. PMRS appears to be using the term ''extraction'' to mean that it is difficult to separate the API from the excipients in solution, not that it is difficult to prepare a solution that contains the API. In fact, PMRS's data show that the oxycodone in its formulation can be readily extracted in commonly available solvents into a solution physically suitable for injection. These data show that more of the API could be extracted from oxycodone HCl IR capsules (approximately 98 percent of the API) than from ROXICODONE (approximately 90–91 percent) in both small and medium volume extraction and at ambient and high temperatures (Refs. 1 and 2).

[2] While PMRS initially intended for the product to confer resistance to grinding to particle sizes suitable for snorting (Ref. 7), PMRS has conceded, based on the results of its testing, that the formulation should not be considered to have this property. See Ref. 2 at 12–13 (''Because of the decrease in particle size distribution after grinding as the drug product ages, resistance to grinding cannot be considered as one of the characteristics of [PMRS' product]'').