



Memorandum

Date: February 1, 2023

To: Government Public Health and Emergency Response Stakeholders

From: Namandjé N. Bumpus, Ph.D., Chief Scientist

Subject: Update on Expiration Date Extensions of Certain Lots of Doxycycline Hyclate 100 mg Capsules Held in Strategic Stockpiles

This memorandum provides an important update about expiration date extensions of certain lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward Pharmaceuticals (West-Ward) held in strategic stockpiles by government public health and emergency response stakeholders for anthrax emergency preparedness and response.

Background

In April 2019, the U.S. Food and Drug Administration (FDA) issued guidance, *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles: Guidance for Government Public Health and Emergency Response Stakeholders* (“guidance”), to help enable government stakeholders to maintain strategic stockpiles of FDA-approved doxycycline tablets and capsules held for public health preparedness for an anthrax emergency response.^{1,2} The guidance describes the doxycycline products that are eligible for expiry dating extensions and provides laboratory testing protocols, enabling government stakeholders to have specific lots of their stockpiled doxycycline tested to determine whether such products would be eligible for an expiration date extension of two (2) years.

As further stated in the guidance, before an identified lot of doxycycline may be used beyond its manufacturer labeled expiration date, FDA first must authorize the extension for that lot based

¹ FDA. *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles: Guidance for Government Public Health and Emergency Response Stakeholders*. April 2019. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/extending-expiration-dates-doxycycline-tablets-and-capsules-strategic-stockpiles>.

² The guidance defines “government stakeholders” as the public health and/or emergency response agencies or their agents/delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundaries (e.g., city, county, tribal, territorial, State, or Federal), or functional range or sphere of authority (e.g., law enforcement, public health, military health) to prescribe, administer, deliver, distribute, hold, or dispense a medical product during an emergency situation.

on a review of a government stakeholder request that includes testing data.^{3,4} If FDA authorizes such a requested expiration dating extension, other government stakeholders holding the same lot(s) of the extended product identified by FDA may apply the same extension of shelf life to their own stockpiled lot(s) of doxycycline without testing such lot(s), so long as such stakeholders follow the applicable requirements and conditions described in Section III.E.4 of the guidance. Among these requirements is that all untested lots held by government stakeholders that apply an authorized extension to such lot(s) must have been stored according to the product's manufacturer labeled storage conditions for the entire time they were stockpiled; if not, the authorized extension will not apply to such untested lot(s).

To date, FDA has received three (3) requests, all of which were submitted by the same government stakeholder in 2018, 2020, and 2022 for the same five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward Pharmaceuticals (West-Ward). These requests are summarized below.⁵

2018 Extension Request

On July 30, 2018, FDA received a government stakeholder request based on the draft guidance to extend the manufacturer labeled expiration date of five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward that had been stockpiled for anthrax preparedness under the manufacturer labeled storage conditions.⁶ The July 30, 2018, request stated that the lots were tested on June 28, 2018, in accordance with the Table 1 Testing Protocol described in Section of III.C.1 of the draft guidance.

Based on the data submitted to FDA in the July 30, 2018, request, FDA concluded in an August

³ Section 564A(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) authorizes FDA to extend the expiration dating of certain eligible stockpiled medical countermeasures (as defined in section 564A(a) of the FD&C Act) intended to support the nation's ability to protect the public health or military preparedness and effectiveness. An expiration date extension must be supported by an appropriate scientific evaluation that is conducted or accepted by FDA. Under this authority, products with extended expiry dates will not be deemed unapproved, adulterated, or misbranded.

⁴ Expiry dating extensions authorized under section 564A(b) of the FD&C Act are limited to the specific products/lots identified by FDA. For purposes of this memorandum, doxycycline is considered an eligible product under section 564A(a) of the FD&C Act because it is an FDA-approved drug, intended for use for anthrax post-exposure prophylaxis or treatment, and intended for use during the circumstances under which a determination of a significant potential for a domestic emergency involving a heightened risk of attack with *B. anthracis*, the biological agent that causes anthrax disease, was made in 2008 by the Secretary of Homeland Security under section 564(b)(1)(A) of the FD&C Act or under which a material threat determination for *B. anthracis* was made in 2004 by the Secretary of Homeland Security.

⁵ In addition, to help inform the development of the April 2019 guidance, as part of a limited pilot study FDA tested certain lots of doxycycline that were beyond their manufacturer labeled expiration date to assess testing methodologies and whether expiration dating extensions of the product might be feasible. Based on its review of appropriate scientific data, FDA concluded that, provided the products had been, and continued to be, properly stored according to the manufacturer's labeled storage conditions, it was scientifically supportable for six (6) specific lots of doxycycline hyclate 100-mg capsules manufactured by West-Ward to continue to be stockpiled and used by stakeholders through the new use dates identified in a September 3, 2015, memorandum. FDA. *Expiry Date Extensions of Certain Lots of Doxycycline Hyclate 100mg Capsules Held in Strategic Stockpiles*. September 3, 2015. <https://www.fda.gov/media/93622/download>.

⁶ FDA. *Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles: Draft Guidance for Government Public Health and Emergency Response Stakeholders*. April 2017. This draft guidance was replaced by final guidance issued by FDA in April 2019 (see Footnote 1).

22, 2018, memorandum that, provided the products had been, and continued to be, properly stored according to the manufacturer’s labeled storage conditions, it was scientifically supportable for the five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward to continue to be stockpiled and used by any government stakeholder through the new use dates (i.e., 2 years from the date of testing) identified in the August 22, 2018, memorandum for anthrax emergency preparedness and response purposes (see Table 1 below).⁷

2020 Extension Request

On July 22, 2020, FDA received a stakeholder request based on the guidance to extend the manufacturer labeled expiration date of five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward that had been stockpiled for anthrax preparedness under the manufacturer labeled storage conditions. These are the same five (5) stakeholder lots that FDA authorized on August 22, 2018, for a 2-year expiration dating extension. The July 22, 2020, request stated that these lots were retested in July 2020 in accordance with the Table 1 Testing Protocol described in Section of III.C.1 of the guidance.

Based on the data submitted to FDA in the July 22, 2020, request, FDA concluded in an August 7, 2020, memorandum that, provided the products had been, and continued to be, properly stored according to the manufacturer’s labeled storage conditions, it was scientifically supportable for the five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward to continue to be stockpiled and used by any government stakeholder through the new use dates (i.e., 2 years from the date of testing) identified in the August 7, 2020, memorandum for anthrax emergency preparedness and response purposes (see Table 1 below).⁸

2022 Extension Request

On September 29, 2022, FDA received a stakeholder request based on the guidance to extend the manufacturer labeled expiration date of five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward that have been stockpiled for anthrax preparedness under the manufacturer labeled storage conditions. These are the same five (5) lots of doxycycline that FDA authorized on August 22, 2018, and on August 7, 2020, for subsequent 2-year expiration dating extensions.

The September 29, 2022, request stated that these lots were retested in July 2022 in accordance with the guidance. Based on the data submitted to FDA in the request, FDA has concluded that it is not scientifically supportable for the five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward that are identified below in Table 1 to continue to be stockpiled and used by the requesting stakeholder. The test results in the September 29, 2022, request do not support an expiry date extension because degradants exceeded acceptable limits. As described in the guidance, from a pharmacology/toxicology perspective, the acceptable limits for degradants in doxycycline tablets and capsules should be restricted to the existing limits in the USP monographs. The requesting stakeholder should properly dispose of this stockpiled product, for example to prevent possible misuse, environmental contamination, or antimicrobial resistance.

⁷ FDA. *Expiration Date Extensions of Certain Lots of Doxycycline Hyclate 100 mg Capsules Held in Strategic Stockpiles*. August 22, 2018. <https://www.fda.gov/media/119947/download>. These 2018 extensions were based on draft guidance issued by FDA in April 2017 (see Footnote 6).

⁸ FDA. *Additional Expiration Date Extensions of Certain Lots of Doxycycline Hyclate 100 mg Capsules Held in Strategic Stockpiles*. August 7, 2020. <https://www.fda.gov/media/141039/download>.

If other government stakeholders properly hold any of the same five (5) lots of doxycycline hyclate 100 mg capsules manufactured by West-Ward listed below in Table 1 and have relied on these lots' 2018 and 2020 expiration dating extensions, then the stakeholder may test their lot(s) to determine whether it would be scientifically supportable for them to continue to store and use the product for anthrax preparedness. If any of the lots listed in Table 1 undergo further testing and are 6 years or more beyond the manufacturer's original labeled expiration date, then it is recommended that the Table 2 Testing Protocol (described in Section of III.C.2 of the guidance) be used. Government stakeholders who do not submit such data to FDA, or who otherwise receive notification from FDA to dispose of their lot(s) after FDA reviews their test data, should properly dispose of this stockpiled product, for example to prevent possible misuse, environmental contamination, or antimicrobial resistance.

Table 1. West-Ward doxycycline hyclate 100 mg capsules eligible for use beyond the manufacturer's labeled expiration date

Doxycycline Lot Number (West-Ward)	Manufacturer's Original Labeled Expiry Date	<u>1st Extension:</u> New Use Date (Issued on August 22, 2018)⁹	<u>2nd Extension:</u> New Use Date (Issued on August 7, 2020)¹⁰	<u>3rd Extension Request (September 2022):</u> No Extension (January 2023)
68788A	March 31, 2015	June 30, 2020	July 31, 2022	N/A
GS008914	March 31, 2018	June 30, 2020	July 31, 2022	N/A
GS008915	March 31, 2018	June 30, 2020	July 31, 2022	N/A
GS008916	April 30, 2018	June 30, 2020	July 31, 2022	N/A
GS008917	April 30, 2018	June 30, 2020	July 31, 2022	N/A

For questions related to this memorandum, please contact Brad Leissa at brad.leissa@fda.hhs.gov or Brooke Courtney at brooke.courtney@fda.hhs.gov.

⁹ FDA. *Expiration Date Extensions of Certain Lots of Doxycycline Hyclate 100 mg Capsules Held in Strategic Stockpiles*. August 22, 2018. <https://www.fda.gov/media/119947/download>.

¹⁰ FDA. *Additional Expiration Date Extensions of Certain Lots of Doxycycline Hyclate 100 mg Capsules Held in Strategic Stockpiles*. August 7, 2020. <https://www.fda.gov/media/141039/download>.