true and complete copy of the petition has been served upon the patent applicant. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41–42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Submit petitions electronically to *https://www.regulations.gov* at Docket No. FDA–2013–S–0610. Submit written petitions (two copies are required) to the Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Dated: September 4, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020–20040 Filed 9–10–20; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–N–1729]

Authorizations and Revocation of Emergency Use of Drugs During the COVID–19 Pandemic; Availability

AGENCY: Food and Drug Administration, Health and Human Services (HHS).

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of four Emergency Use Authorizations (EUAs) (the Authorizations) for drugs for use during the COVID–19 pandemic. FDA issued four Authorizations under the Federal Food, Drug, and Cosmetic Act (FD&C Act), as requested by the Department of Health and Human Services (HHS) Biomedical Advanced Research and Development Authority (BARDA), Fresenius Medical Care, Gilead Sciences, Inc., and Fresenius Kabi USA, LLC. The Authorizations contain, among other things, conditions on the emergency use of the authorized drugs. The Authorizations follow the February 4, 2020, determination by the Secretary of HHS that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves a novel (new) coronavirus. The virus is now named SARS-CoV–2, which causes the illness COVID–19. On the basis of such determination, the Secretary of HHS declared on March 27, 2020, that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID–19 pandemic, pursuant to the FD&C Act, subject to the terms of any authorization issued under that section. FDA is also announcing the subsequent revocation of the Authorization issued to BARDA for oral formulations of chloroquine phosphate and hydroxychloroquine sulfate. FDA revoked this authorization on June 15, 2020. The Authorizations, and the revocation, which include an explanation of the reasons for issuance or revocation, are reprinted in this document.

DATES: The Authorization for BARDA was effective as of March 28, 2020, and the revocation of this Authorization is effective as of June 15, 2020; the Authorization for Fresenius Medical Care is effective as of April 30, 2020; the Authorization for Gilead Sciences, Inc. is effective as of May 1, 2020; the Authorization for Fresenius Kabi USA, LLC is effective as of May 8, 2020.

ADDRESSES: Submit written requests for single copies of the EUAs to the Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, Rm. 4338, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your request or include a Fax number to which the Authorizations may be sent. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the Authorizations.

FOR FURTHER INFORMATION CONTACT: Michael Mair, Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, Rm. 4332, Silver Spring, MD 20993–0002, 301–796–8510 (this is not a toll free number).

SUPPLEMENTARY INFORMATION:

I. Background

Section 564 of the FD&C Act (21 U.S.C. 360bbb–3) allows FDA to strengthen the public health protections against biological, chemical, nuclear, and radiological agents. Among other things, section 564 of the FD&C Act allows FDA to authorize the use of an unapproved medical product or an unapproved use of an approved medical product in certain situations. With this EUA authority, FDA can help ensure that medical countermeasures may be used in emergencies to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by biological, chemical, nuclear, or radiological agents when there are no adequate, approved, and available alternatives.

II. Criteria for EUA Authorization

Section 564(b)(1) of the FD&C Act provides that, before an EUA may be issued, the Secretary of HHS must declare that circumstances exist justifying the authorization based on one of the following grounds: (1) A determination by the Secretary of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents; (2) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to U.S. military forces, including personnel operating under the authority of title 10 or title 50, United States Code, of attack with (i) a biological, chemical, radiological, or nuclear agent or agents; or (ii) an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces;[1] (3) a determination by the Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of U.S. citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such agent or agents; or (4) the identification of a material threat by the Secretary of Homeland Security pursuant to section 319F–2 of the Public Health Service (PHS) Act (42 U.S.C. 247d–6b) sufficient to affect national security or the health and security of U.S. citizens living abroad.

Once the Secretary of HHS has declared that circumstances exist justifying an authorization under section 564 of the FD&C Act, FDA may authorize the emergency use of a drug, device, or biological product if the Agency concludes that the statutory criteria are satisfied. Under section 564(h)(1) of the FD&C Act, FDA is required to publish in the **Federal Register** a notice of each authorization, and each termination or revocation of an authorization, and an explanation of the reasons for the action. Section 564 of the FD&C Act permits FDA to authorize the introduction into interstate commerce of

[1] In the case of a determination by the Secretary of Defense, the Secretary of HHS shall determine within 45 calendar days of such determination, whether to make a declaration under section 564(b)(1) of the FD&C Act, and, if appropriate, shall promptly make such a declaration.

a drug, device, or biological product intended for use when the Secretary of HHS has declared that circumstances exist justifying the authorization of emergency use. Products appropriate for emergency use may include products and uses that are not approved, cleared, or licensed under sections 505, 510(k), 512, or 515 of the FD&C Act (21 U.S.C. 355, 360(k), 360b, and 360e) or section 351 of the PHS Act (42 U.S.C. 262), or conditionally approved under section 571 of the FD&C Act (21 U.S.C. 360ccc). FDA may issue an EUA only if, after consultation with the HHS Assistant Secretary for Preparedness and Response, the Director of the National Institutes of Health, and the Director of the Centers for Disease Control and Prevention (to the extent feasible and appropriate given the applicable circumstances), FDA [2] concludes: (1) That an agent referred to in a declaration of emergency or threat can cause a serious or life-threatening disease or condition; (2) that, based on the totality of scientific evidence available to FDA, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that: (A) The product may be effective in diagnosing, treating, or preventing (i) such disease or condition; or (ii) a serious or life-threatening disease or condition caused by a product authorized under section 564, approved or cleared under the FD&C Act, or licensed under section 351 of the PHS Act, for diagnosing, treating, or preventing such a disease or condition caused by such an agent; and (B) the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product, taking into consideration the material threat posed by the agent or agents identified in a declaration under section 564(b)(1)(D) of the FD&C Act, if applicable; (3) that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition; (4) in the case of a determination described in section 564(b)(1)(B)(ii), that the request for emergency use is made by the Secretary of Defense; and (5) that such other criteria as may be prescribed by regulation are satisfied.

No other criteria for issuance have been prescribed by regulation under section 564(c)(4) of the FD&C Act.

III. The Authorizations

The Authorizations follow the February 4, 2020, determination by the Secretary of HHS that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves a novel (new) coronavirus. The virus is now named SARS-CoV–2, which causes the illness COVID–19. Notice of the Secretary's determination was provided in the **Federal Register** on February 7, 2020 (85 FR 7316). On the basis of such determination, the Secretary of HHS declared on March 27, 2020, that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID–19 pandemic, pursuant to section 564 of the FD&C Act, subject to the terms of any authorization issued under that section. Notice of the Secretary's declaration was provided in the **Federal Register** on April 1, 2020 (85 FR 18250). Having concluded that the criteria for issuance of the Authorizations under section 564(c) of the FD&C Act are met, FDA has issued four authorizations for the emergency use of drugs during the COVID–19 pandemic. On March 28, 2020, FDA issued an EUA to BARDA for oral formulations of chloroquine phosphate and hydroxychloroquine sulfate, subject to the terms of the Authorization. On April 30, 2020, FDA issued an EUA to Fresenius Medical Care for multiFiltrate PRO System and multiBic/multiPlus Solutions, subject to the terms of the Authorization. On May 1, 2020, FDA issued an EUA to Gilead Sciences, Inc. for remdesivir, subject to the terms of the Authorization. On May 8, 2020, FDA issued an EUA to Fresenius Kabi USA, LLC for Fresenius Propoven 2% Emulsion, subject to the terms of the Authorization. The Authorizations in their entirety (not including the authorized versions of the fact sheets and other written materials) follow, below section VI Electronic Access, and provide an explanation of the reasons for issuance, as required by section 564(h)(1) of the FD&C Act.

IV. EUA Criteria for Issuance No Longer Met

Under section 564(g)(2) of the FD&C Act, the Secretary of HHS may revoke an EUA if, among other things, the criteria for issuance are no longer met. On June 15, 2020, FDA revoked the EUA for BARDA for oral formulations of chloroquine phosphate and hydroxychloroquine sulfate because the criteria for issuance were no longer met. Under section 564(c)(2) of the FD&C Act, an EUA may be issued only if FDA concludes that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that: (1) The product may be effective in diagnosing, treating, or preventing such disease or condition and (2) the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product. Based on a review of new information and a reevaluation of information available at the time the EUA was issued, FDA now concludes it is no longer reasonable to believe that (1) oral formulations of chloroquine phosphate and hydroxychloroquine sulfate may be effective in treating COVID–19 for the uses authorized in the EUA, or (2) the known and potential benefits of these products outweigh their known and potential risks for those uses. Accordingly, FDA revokes the EUA for emergency use of chloroquine phosphate and hydroxychloroquine sulfate to treat COVID–19, pursuant to section 564(g)(2) of the FD&C Act.

V. The Revocation

Having concluded that the criteria for revocation of the Authorization under section 564(g) of the FD&C Act are met, FDA has revoked the EUA for BARDA's oral formulations of chloroquine phosphate and hydroxychloroquine sulfate. The revocation in its entirety follows, below section VI. Electronic Access, and provides an explanation of the reasons for revocation, as required by section 564(h)(1) of the FD&C Act.

VI. Electronic Access

An electronic version of this document and the full text of the Authorizations and revocation are available on the internet at *https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.*

BILLING CODE 4164–01–P

[2] The Secretary of HHS has delegated the authority to issue an EUA under section 564 of the FD&C Act to the Commissioner of Food and Drugs.

U.S. FOOD & DRUG ADMINISTRATION

March 28, 2020

Dr. Rick Bright, Ph.D.
Director
Biomedical Advanced Research and Development Authority (BARDA)
Office of Assistant Secretary for Preparedness and Response (ASPR)
U.S. Department of Health and Human Services (HHS)
330 Independence Ave, S.W.
Room 640G
Washington, D.C. 20201

Re: Request for Emergency Use Authorization For Use of Chloroquine Phosphate or Hydroxychloroquine Sulfate Supplied From the Strategic National Stockpile for Treatment of 2019 Coronavirus Disease

Dear Dr. Bright:

Revoked

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of oral formulations of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of 2019 coronavirus disease (COVID-19) when administered by a healthcare provider (HCP)[1] pursuant to a valid prescription of a licensed practitioner as described in the Scope of Authorization (section II) of this letter. The authorized chloroquine phosphate and hydroxychloroquine sulfate are limited to product supplied from the Strategic National Stockpile (SNS) to public health authorities[2], pursuant to Section 564 of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[3,4] Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS

[1] For purposes of this EUA, the term "healthcare provider" means licensed healthcare professionals who are acting within their professional scope of practice under the public health authority of official emergency response plans when administering the authorized product.

[2] "Public health authority" means the public agency or its delegate that has legal responsibility and authority for responding to a public health emergency, based on political or geographical (e.g., city, county, tribal, State, or Federal) or functional (e.g., law enforcement or public health range) or sphere of authority to prescribe, administer, deliver, distribute, or dispense oral chloroquine phosphate and hydroxychloroquine sulfate products during public health emergencies.

[3] On February 11, 2020, the virus tentatively named 2019-nCoV was formally designated as Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Also on February 11, 2020, the disease caused by SARS-CoV-2 was

then declared that circumstances exist justifying the authorization of emergency use of drugs and biologics during the COVID-19 outbreak, pursuant to section 564 of the Act, subject to terms of any authorization issued under that section.[5]

Chloroquine phosphate and hydroxychloroquine sulfate are not FDA-approved for treatment of COVID-19. Some versions of chloroquine phosphate are approved by FDA for other indications—for prophylaxis and acute attacks of certain strains of malaria and for the treatment of extraintestinal amebiasis, but the chloroquine phosphate drug product covered by this letter has not been approved. Several versions of hydroxychloroquine sulfate are approved by FDA for prophylaxis of and treatment of malaria, treatment of lupus erythematosus, and treatment of rheumatoid arthritis. The safety profile of these drugs has only been studied for FDA approved indications, not COVID-19.

Based upon limited in-vitro and anecdotal clinical data in case series, chloroquine phosphate and hydroxychloroquine sulfate are currently recommended for treatment of hospitalized COVID-19 patients in several countries, and a number of national guidelines report incorporating recommendations regarding use of chloroquine phosphate or hydroxychloroquine sulfate in the setting of COVID-19. FDA encourages the conduct and participation in randomized controlled clinical trials that may produce evidence concerning the effectiveness of these products in treating COVID-19. FDA is issuing this EUA to facilitate the availability of chloroquine phosphate and hydroxychloroquine sulfate during the COVID-19 pandemic to treat patients for whom a clinical trial is not available, or participation is not feasible.

Revoked

Having concluded that the criteria for issuance of this authorization under 564(c) of the Act are met, I am authorizing the emergency use of chloroquine phosphate and hydroxychloroquine sulfate, as described in the Scope of Authorization section of this letter (Section II) for treatment of COVID-19 when clinical trials are not available, or participation is not feasible, subject to the terms of this authorization.

Clinical trial data results, and any information derived from clinical trials, as well as clinical trial results from studies of other investigational medical products to treat COVID-19, will continue to inform this risk benefit assessment.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19 when administered as described in the Scope of Authorization (section II) meet the criteria for issuance of an authorization under Section 564(c) of the Act, because:

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formally designated as Coronavirus Disease 2019 (COVID-19). This document uses the updated names.

[4] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. February 4, 2020.*

[5] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. March 27, 2020.*

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that chloroquine phosphate and hydroxychloroquine sulfate may be effective in treating COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of chloroquine phosphate and hydroxychloroquine sulfate when used to treat COVID-19 outweigh the known and potential risks of such products; and
3. There is no adequate, approved, and available alternative to the emergency use of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19.[6]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19, as described in this section.

Authorized Chloroquine Phosphate

Revoked

I am authorizing use of the following chloroquine phosphate product that is distributed from the SNS to public health authorities for response to the COVID-19 pandemic:

- Chloroquine phosphate that is not approved by FDA for any indication.[7]
- The chloroquine phosphate must be administered by a healthcare provider pursuant to a valid prescription of a licensed practitioner.
- The chloroquine phosphate may only be used to treat adult and adolescent patients who weigh 50 kg or more and are hospitalized with COVID-19, for whom a clinical trial is not available, or participation is not feasible.[8]

The product is authorized to be accompanied by the following product-specific information pertaining to emergency use, which is required to be made available to healthcare providers and patients respectively:

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[6] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

[7] The authorized chloroquine phosphate may be accompanied by a package insert that is not approved labeling in the United States. Instead, refer to the authorized Fact Sheet for Healthcare Providers: Use of Chloroquine Phosphate Supplied from the Strategic National Stockpile for treatment of COVID-19 in Certain Hospitalized Patients. Note that Chloroquine phosphate's U.S. labeling that is FDA-approved for other indications, not COVID-19, does not include information regarding safety or effectiveness for COVID-19, see: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f398f8a9-92f3-47cb-81c2-6078806a464d

[8] For a listing of clinical trials, see: https://clinicaltrials.gov/

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) of Chloroquine Phosphate Supplied from the Strategic National Stockpile for Treatment of COVID-19 in Certain Hospitalized Patients
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Chloroquine Phosphate For Treatment of COVID-19 in Certain Hospitalized Patients

The above described products are authorized to be administered under this EUA despite the fact that they do not meet certain requirements otherwise required by applicable federal law.

Authorized Hydroxychloroquine Sulfate

I am authorizing use of the following hydroxychloroquine sulfate product that is distributed from the SNS to public health authorities for response to the COVID-19 pandemic:

- FDA-approved hydroxychloroquine sulfate that is approved by FDA for other uses and accompanied by its FDA-approved labeling and authorized Fact Sheets.

- The hydroxychloroquine sulfate must be administered by a healthcare provider pursuant to a valid valid prescription of a licensed practitioner.

- The hydroxychloroquine sulfate may only be used to treat adult and adolescent patients who weigh 50 kg or more hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.[9]

Revoked

The product is authorized to be accompanied by the product information contained in hydroxychloroquine sulfate's approved package insert (for other indications)[10] and together with the following product-specific information pertaining to emergency use, which is required to be made available to healthcare providers and patients respectively:

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) of Hydroxychloroquine Sulfate Supplied from the Strategic National Stockpile for Treatment of COVID-19 in Certain Hospitalized Patients
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Hydroxychloroquine Sulfate For Treatment of COVID-19 in Certain Hospitalized Patients

The above described product, when labeled consistently with the labeling of this product for its approved uses is authorized to be distributed to and administered under this EUA despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of chloroquine phosphate and hydroxychloroquine sulfate, when used for the treatment of SARS-CoV-2 and used consistently with the Scope of

[9] For a listing of clinical trials, see: https://clinicaltrials.gov/

[10] For hydroxychloroquine's package insert, see: https://dailymed.nlm.nih.gov/dailymed/

Authorization of this letter (Section II), outweigh the known and potential risks of these products.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that chloroquine phosphate and hydroxychloroquine sulfate may be effective for the treatment of COVID-19, when used consistently with the Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I of this letter, I have concluded that chloroquine phosphate and hydroxychloroquine sulfate (as described in the Scope of Authorization of this letter (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of these products under an EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), these products are authorized for the treatment of 2019 coronavirus disease (COVID-19) when administered by a HCP pursuant to a valid prescription of a licensed practitioner as described in the Scope of Authorization (section II) of this letter.

Revoked

The EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under Section 564(b)(2) of the Act or when the EUA is revoked under Section 564(g) of the Act.

III. Waiver of Certain Requirements

Pursuant to Section 564(e)(3) of the Act, with respect to the emergency use of a product for which an authorization under this section is issued, FDA may waive or limit, to the extent appropriate given the circumstances of the emergency, requirements regarding current good manufacturing practice otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulation under this Act, including such requirements established under Section 501. FDA grants that waiver with respect to the products covered by this authorization.

IV. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

A. SNS will distribute the authorized chloroquine phosphate and hydroxychloroquine sulfate under its direction to the extent such distributions are consistent with and do not exceed the terms of this letter, including distribution with the authorized labeling.

B. Through a process of inventory control, SNS will maintain records regarding distribution under its direction of the authorized chloroquine phosphate and hydroxychloroquine sulfate (i.e., lot numbers, quantity, receiving site, receipt date).

C. HHS will ensure that the terms of this EUA are made available to public health authorities through appropriate means.[11] HHS will provide public health authorities a copy of this letter of authorization and communicate to public health authorities any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (e.g., Fact Sheets).

D. BARDA, ASPR, or other organization within HHS may request the authorization of additional chloroquine phosphate and hydroxychloroquine sulfate products under this EUA. Additional such products may be included in this authorization, without amendment of this EUA, upon concurrence of, Office of Infectious Diseases/OND/CDER, CTECS/OCD/CDER, and OCET/OCS/OC.

E. BARDA may request changes to this authorization, including to the authorized fact sheets for chloroquine phosphate and hydroxychloroquine sulfate products and to require patient outcomes reporting if and when a system is established, without amendment of this EUA, upon concurrence of, Office of Infectious Diseases /OND/CDER, CTECS/OCD/CDER, and OCET/OCS/OC.

F. HHS will inform public health authorities about the need to have a process in place for performing adverse event monitoring and compliance activities designed to ensure that adverse events and all medication errors associated with the use of the authorized chloroquine phosphate or hydroxychloroquine sulfate are reported to FDA, to the extent practicable given emergency circumstances, as follows: complete the MedWatch FDA Form online at www.fda.gov/medwatch/report.htm, or by using a postage-paid MedWatch Form 3500 (available at https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home), or by calling 1-800-FDA-1088. Submitted reports should state: "use of chloroquine phosphate was under an EUA" or "use of hydroxychloroquine sulfate was under an EUA," as relevant. If and when HHS establishes a process for collecting outcomes data, HHS will inform public health authorities about such process.

G. SNS will ensure that the authorized chloroquine phosphate and hydroxychloroquine sulfate is distributed for use under its direction within the expiry dating on the manufacturer's labeling. If FDA authorizes any expiry dating extensions of the authorized chloroquine phosphate or hydroxychloroquine sulfate under this EUA, SNS will inform emergency response stakeholders receiving the authorized chloroquine phosphate or hydroxychloroquine sulfate of such extensions and any conditions related to such extensions under this EUA. SNS will maintain adequate records regarding the expiry dates by which authorized chloroquine phosphate and hydroxychloroquine sulfate may be used.

Revoked

[11] For example, through hard copy, web posting, and/or mass media.

H. SNS will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Systems to Whom the Authorized Chloroquine Phosphate and Hydroxychloroquine Sulfate Is Distributed

I. Healthcare systems and healthcare providers receiving the chloroquine phosphate and/or hydroxychloroquine sulfate from the SNS will track adverse events and report to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit a MedWatch form (www.fda.gov/medwatch/report.htm), or Complete and submit FDA Form 3500 (health professional) or FDA Form 3500B (consumer/patient) by fax (1-800-FDA-0178). These forms can be found via link above. Call 1-800-FDA-1088 for questions. Submitted reports should state "chloroquine phosphate treatment under EUA" or "hydroxychloroquine sulfate treatment under EUA."

J. Through a process of inventory control, healthcare systems will maintain records regarding the dispensed authorized chloroquine phosphate and hydroxychloroquine sulfate (i.e., lot numbers, quantity, receiving site, receipt date) and maintain patient information and other relevant data as feasible (e.g., patient name, age, disease manifestation, other drugs administered, outcomes).

K. Healthcare systems will ensure that any records associated with this EUA are maintained until notified by SNS and/or FDA. Such records will be made available to FDA, SNS and BARDA for inspection upon request.

Revoked

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

/s/

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures

April 30, 2020

Denise Oppermann
Fresenius Medical Care
920 Winter Street
Waltham, MA 02451

Dear Denise Oppermann:

This letter is in response to Fresenius Medical Care's request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the multiFiltrate PRO System[1] and multiBic/multiPlus Solutions[2] to provide continuous renal replacement therapy (CRRT) to treat patients in an acute care environment during the Coronavirus Disease 2019 (COVID-19) pandemic, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[3] Pursuant to section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared on March 24, 2020, that circumstances exist justifying the authorization of emergency use of medical devices, including alternative products used as medical devices, due to shortages during the COVID-19 outbreak, subject to the terms of any authorization issued under that section.[4] Again pursuant to section 564 and on the same basis, the Secretary of HHS declared on March 27, 2020, that circumstances exist justifying the

[1] The multiFiltrate PRO System includes the multiFiltrate PRO delivery unit, the Ultraflux AV 400S/600S/1000S hemodialyzers/hemofilters, and the multiFiltrate PRO hemodiafiltration cassette (bloodline/tubing systems for blood purification). All components of the system have a current CE (European Conformity) mark. The multiFiltrate PRO system, including any device accessories, are devices regulated by the Center for Devices and Radiological Health (CDRH).

[2] The multiBic/multiPlus Solutions include multiBic dialysate and replacement fluid and multiPlus dialysate. All of these solutions are authorized for marketing in the European Union. The multiBic dialysate and the multiPlus dialysate solutions are regulated as devices by CDRH. The multiBic replacement fluid is regulated as a drug by the Center for Drug Evaluation and Research (CDER). The composition of the solutions can be referenced in tables 1 and 2 of this authorization letter.

[3] U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 7, 2020).

[4] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 17335 (March 27, 2020).

authorization of emergency use of drugs and biological products during the COVID-19 pandemic, subject to the terms of the authorization issued under that section.[5]
Based on published data from China and preliminary reports in the U.S., it has been noted that SARS-CoV-2, the virus that causes COVID-19, has led to an increased population with critical illness and multiple organ failure, including acute kidney injury, increasing the need for CRRT. As a result, there is a shortage of devices, accessories and solutions to provide CRRT in critically ill patients. Based on the totality of scientific evidence available, FDA has concluded that the multiFiltrate PRO System and multiBic/multiPlus Solutions may be effective in providing CRRT in an acute care environment and in turn, may provide clinical benefit during the shortage situation.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act are met, I am authorizing the emergency use of your MultiFiltrate PRO System and multiBic/multiPlus Solutions, as described in the Scope of Authorization (Section II) of this letter, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the multiFiltrate PRO System device and multiBic/multiPlus Solutions, as described in the Scope of Authorization (Section II) of this letter to provide CRRT in an acute care environment, meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. SARS-CoV-2, the virus that causes COVID-19, can cause a serious or life-threatening disease or condition, including severe respiratory illness and multiple organ failure, including acute kidney injury, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your multiFiltrate PRO System and multiBic/multiPlus Solutions may be effective in delivering CRRT in an acute care environment, and that the known and potential benefits of the multiFiltrate PRO System and multiBic/multiPlus Solutions, when used for the indication above, outweigh the known and potential risks of the multiFiltrate PRO System and multiBic/multiPlus Solutions; and

3. There is no adequate, approved, and available alternative to the emergency use of the multiFiltrate PRO System and the multBic/multiPlus Solutions when there are shortages of FDA-approved alternatives during the COVID-19 pandemic.[6]

II. Scope of Authorization

[5] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).
[6] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the multiFiltrate PRO System and multiBic/multiPlus Solutions to deliver CRRT to treat patients in an acute care environment during the COVID-19 pandemic.

Authorized Product Details

The multiFiltrate PRO System is designed to provide CRRT by controlling and monitoring extracorporeal blood and fluid circuits.

The following CRRT modalities are available with the multiFiltrate PRO System:

- CVVHD - Continuous Veno Venous Hemodialysis
- CVVH - Continuous Veno Venous Hemofiltration, with pre-dialyzer dilution, post-dialyzer dilution, and pre-post-dialyzer dilution
- CVVHDF - Continuous Veno Venous Hemodiafiltration, with both pre-dialyzer dilution and post dialyzer dilution

MultiFiltrate PRO System Components

multiFiltrate PRO Delivery Unit

A high-resolution touchscreen monitor and four mechanical buttons allow the user to view, monitor, and input or change parameters to manage the treatment. In the extracorporeal blood circuit, blood is pumped from the patient, through a dialyzer attached to the tubing cassette and back to the patient. Blood, filtrate, dialysate, replacement fluid and heparin pumps are used as indicated to meet individual patient's needs and various therapy modes. There is a range of options for delivering CRRT with pre-dialyzer, post-dialyzer or pre- and post-dialyzer dilution. Fluid balance is achieved via scale-based technology. Integrated heaters can be used to heat the dialysate and/or replacement fluids as necessary.

There are a total of four scales for continuous control of fluid. Scales 1 and 2 weigh the dialysates and/or replacement fluids. Scales 3 and 4 weigh the filtrate. The difference between these two sets of scales is monitored to control the fluid balance. The maximum load capacity of each scale is 12 Kg, allowing the user to load as much as 10 L of treatment solution per scale. Handles are located on the front and on the back for ease in transporting the device. The card slot allows for role-dependent access to machine functionality.

Disposable Bloodline/Tubing

The multiFiltrate PRO Hemodiafiltration (HDF) Cassette is used for any treatment modality with heparin anticoagulation.

Hemodialyzers/Hemofilters

Three models of the ultrafluX AV-series dialyzers are used with the system:

- AV-400
- AV-600
- AV-1000

Solutions

Dialysate Solutions

multiBic and multiPlus dialysate Solutions are provided in a two-compartment bag. One compartment contains 4.75L of a slightly alkaline hydrogen carbonate solution. The second compartment contains 0.25L of an acidic electrolyte, glucose solution. The two solutions are combined before use by opening the peel seam between the two compartments, yielding 5L of a ready-to-use sterile solution.

The dialysate bags are made of Biofine SiOx gas barrier foil, an environmentally friendly material which is manufactured without PVC, latex or DEHP. multiBic dialysate solutions are used for hemodialysis and hemodiafiltration modalities (Table 1).

Table 1: multiBic / multiPlus Dialysate Composition

	multiBic	multiPlus
Sodium (Na+) (mmol/L)	140	140
Potassium (K+) (mmol/L)	0, 2, 3, or 4	2
Magnesium (Mg2+) (mmol/L)	0.5	0.75
Calcium (Ca2+) (mmol/L)	1.5	1.5
Chloride (Cl-) (mmol/l)	109, 111, 112, or 113	110.5
Bicarbonate (HCO3-) (mmol/L)	35	35
Phosphate (mmol/L)	0	1
Glucose (mmol/L)	5.55	5.55

Replacement Fluids

Replacement solutions are regulated as drugs by the FDA. Labeling for products used exclusively as dialysate (e.g., multiPlus) contraindicates the use of dialysate solutions as replacement solutions (i.e. direct infusion into the bloodstream).

multiBic replacement solutions are provided in a two-compartment bag. One compartment contains 4.75L of a slightly alkaline hydrogen carbonate solution. The second compartment contains 0.25L of an acidic electrolyte, glucose solution. The two solutions are combined before use by opening the peel seam between the two compartments, yielding 5L of a ready-to-use sterile solution.

The bags are made of Biofine SiOx gas barrier foil, an environmentally friendly material which is manufactured without PVC, latex or DEHP. multiBic Solutions are used for hemodialysis, hemofiltration and hemodiafiltration modalities (Table 2).

Table 2: multiBic Replacement Fluid Composition

Sodium (Na+) (mmol/L)	140
Potassium (K+) (mmol/L)	0, 2, 3, or 4
Magnesium (Mg2+) (mmol/L)	0.5
Calcium (Ca2+) (mmol/L)	1.5
Chloride (Cl-) (mmol/L)	109, 111, 112, or 113
Bicarbonate (HCO3-) (mmol/L)	35
Phosphate (mmol/L)	0
Glucose (mmol/L)	5.55

Performance

The multiFiltrate PRO System and the multiBic/multiPlus Dialysate Solutions comply with the following standards:

- EN ISO 13485:2016 – Medical Devices – Quality Management Systems
- EN ISO 9001:2015 – Quality Management Systems
- MDD 93/42/CE
- ISO 11607-1:2019 - Packaging for terminally sterilized medical devices -- Part 1: Requirements for materials, sterile barrier systems and packaging systems
- ISO 11607-2:2019 - Packaging for terminally sterilized medical devices -- Part 2: Validation requirements for forming, sealing and assembly processes
- EN 1041:2008+A1:2013 – Information supplied by the manufacturer of medical devices
- EN ISO 15223-1:2016 – Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements
- EN 556-1:2001/AC:2006 - Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices
- ISO10993 series – Biological evaluation of medical devices
- EN ISO 14971:2012 Medical devices - Application of risk management to medical devices (ISO 14971:2007, Corrected version 2007-10-01)
- IEC 60601-1: 2005 + CORR.1:2006 + CORR.2:2007 + AM1:2012 - Medical electrical equipment - Part 1: General requirements for basic safety and essential performance
- IEC 60601-1-2: 2014 - Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances - Requirements and tests
- IEC 60601-2-16 Edition 5.0 2018-4 - Medical electrical equipment - Part 2-16: Particular requirements for the basic safety and essential performance of haemodialysis, haemodiafiltration and haemonfiltration equipment
- EN ISO 8637-1: 2017 – Extracorporeal systems for blood purification – Part 1: Haemodialyzers, haemodiafilters, haemofilters and haemoconcentrators
- EN ISO 8637-2:2018 Extracorporeal systems for blood purification - Part 2: Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters (ISO

8637-2:2018)

- EN 1707:1996 - Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment. Lock fittings
- EN ISO 80369-7:2017 Small-bore connectors for liquids and gases in healthcare applications – Part 7: Connectors for intravascular or hypodermic applications (ISO 80369-7:2016, Corrected version 2016-12-01)
- EN ISO 80369-20:2015 Small-bore connectors for liquids and gases in healthcare applications - Part 20: Common test methods (ISO 80369-20:2015)

MultiBic/multPlus replacement solutions

- All applicable European Pharmacopoeial (Ph. Eur.) and/or USP/NF standards.

The multiFiltrate PRO System and multiBic/multiPlus Solutions, when labeled consistently with the labeling authorized by FDA entitled "multiFiltrate PRO Instructions for Use," "Bloodline/Tubing systems for blood purification - Instructions for Use," "Ultraflux AV400S/600S/1000S Instructions for Use," "multiPlus Instructions for Use," and the "Summary of Product Characteristics (SmPC)" for the multiBic Solutions, (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations),[7] is authorized under the terms and conditions of this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

Your multiFiltrate PRO System and multiBic/multiPlus Solutions are authorized to be accompanied by the following product-specific information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Personnel: Emergency Use of multiFiltrate PRO System and multiBic/multiPlus Solutions during the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of multiFiltrate PRO System and multiBic/multiPlus Solutions during the COVID-19 Pandemic

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the multiFiltrate PRO System and multiBic/multiPlus Solutions, when used for CRRT in an acute care environment and used consistently within the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your multiFiltrate PRO System and multiBic/multiPlus Solutions.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the multiFiltrate PRO System and multiBic/multiPlus Solutions may be effective in providing CRRT in an acute care environment, when used consistently with the Scope of Authorization of this letter (Section II), pursuant to section 564(c)(2)(A) of the Act.

[7] As part of this authorization, the multiFiltrate PRO System and multiBic/multiPlus Solutions will be distributed with the labeling that accompanies these products for distribution in the European Union.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that the multiFiltrate PRO System and multiBic/multiPlus Solutions, when used to provide CRRT in an acute care environment (as described in the Scope of Authorization of this letter (Section II)), meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized products under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the multiFiltrate PRO System and multiBic/multiPlus Solutions, with the required labeling set forth in this section (Section II), are authorized to provide CRRT in an acute care environment.

III. Waiver of Certain FDA Requirements

I am waiving applicable current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the authorized devices, including the multiFiltrate PRO System, and multiBic dialysate and multiPlus dialysate Solutions, that are used in accordance with this EUA Conditions of Authorization.

IV. Conditions of Authorization

Pursuant to section 564(e) of the Act, I am establishing the following conditions on this authorization:

Fresenius Medical Care

A. Fresenius Medical Care may request changes to the authorized labeling and fact sheets. Such requests will be made in consultation with, and require concurrence of, the Division of Renal, Gastrointestinal, Obesity and Transplant Devices (DHT3A)/Office of GastroRenal, ObGyn, General Hospital and Urology Devices (OHT3)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) or the Division of Cardiology and Nephrology (DCN)/Office of Cardiology, Hematology, Endocrinology, and Nephrology (OCHEN)/Office of New Drugs (OND)/Center for Drug Evaluation and Research (CDER), as appropriate.

B. Fresenius Medical Care may request changes to the components and materials. Such requests will be made in consultation with, and require concurrence of, DCN/OCHEN/OND/CDER or DHT3A/OHT3/OPEQ/CDRH, as appropriate.

C. Fresenius Medical Care may request changes to the Scope of Authorization (Section II in this letter) of the product. Such requests will be made in consultation with, and require concurrence of, the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC), the DCN/OCHEN/OND/CDER, and the DHT3A/OHT3/OPEQ/CDRH.

D. Fresenius Medical Care may request the addition of other instruments and associated software for use with the product. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH.

E. For the multiBic Solutions used as a replacement solution, Fresenius Medical Care will continue to manufacture the multiBic Solutions in compliance with EU good manufacturing practice (GMP) and pursuant to the European Medicines Agency (EMA) marketing authorization.

F. Fresenius Medical Care will have a process in place to collect information on the performance of the multiFiltrate PRO System and multiBic dialysate and multiPlus dialysate Solutions and for reporting adverse events of which they become aware to FDA under 21 CFR Part 803. Adverse events of which the Fresenius Medical Care becomes aware will be reported to FDA.

G. For the multiBic Solutions when used as replacement solution, Fresenius Medical Care should have a process in place to ensure that adverse events and all medication errors associated with the use of the authorized multiBic Solutions reported to Fresenius Medical Care are reported to FDA, to the extent practicable given emergency circumstances. Prescribing health care providers or designee may report adverse events related to the use of multiBic Solutions during the pandemic to the FDA MedWatch system using one of the following methods:
   - Complete and submit the report online: https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home, or
   - By using a postage-paid Form FDA 3500 (available at https://www.fda.gov/safety/medical-product-safety-information/medwatch-forms-fda-safety-reporting

   Submitted reports should state: "use of multiBic Solution was under an EUA".

H. Fresenius Medical Care is authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.

I. Fresenius Medical Care will notify FDA of any authorized distributor(s) of the product, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA.

Fresenius Medical Care and Authorized Distributor(s)[8]

J. Fresenius Medical Care and authorized distributor(s) will make multiFiltrate PRO System devices and multiBic/multiPlus Solutions available with the authorized labeling and fact sheets, described in the Scope of Authorization (Section II) of this letter.

K. Fresenius Medical Care and authorized distributor(s) will make available on their website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.

[8] "Authorized Distributor(s)" are identified by the sponsor in EUA requests as an entity allowed to distribute the product.

L. Fresenius Medical Care and authorized distributor(s) will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

M. Through a process of inventory control, Fresenius Medical Care and authorized distributor(s) will maintain records of the healthcare settings to which they distribute the multiFiltrate PRO System and multiBic/multiPlus Solutions and number of multiFiltrate PRO Systems and multiBic/multiPlus Solutions they distribute.

N. Fresenius Medical Care and authorized distributor(s) are authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.

Conditions Related to Printed Matter, Advertising and Promotion

O. All descriptive printed matter, including advertising and promotional material, relating to the use of the multiFiltrate PRO System device and multiBic/multiPlus Solutions shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

P. No descriptive printed matter, including advertising or promotional material, relating to the use of the multiFiltrate PRO System and multiBic/multiPlus Solutions may represent or suggest that such products are safe or effective for the delivery of CRRT in an acute care environment.

Q. All descriptive printed matter, including advertising and promotional material, relating to the use of the multiFiltrate PRO System device and multiBic/multiPlus Solutions clearly and conspicuously shall state that:

- the multiFiltrate PRO System device and multiBic/multiPlus Solutions have neither been cleared or approved to provide CRRT in an acute care environment;
- the multiFiltrate PRO System device and multiBic/multiPlus Solutions have been authorized by FDA under an EUA;
- the multiFiltrate PRO System device and multiBic/multiPlus Solutions are authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the multiFiltrate PRO System device and multiBic/multiPlus Solutions under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

V. Duration of Authorization

This EUA will be effective until the declarations that circumstances exist justifying the authorization of the emergency use of the multiFiltrate PRO System and multiBic/multiPlus

solutions during the COVID-19 pandemic are terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures

U.S. FOOD & DRUG ADMINISTRATION

May 1, 2020

Ashley Rhoades, MBS, RAC
Senior Associate, Regulatory Affairs
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Rhoades:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of remdesivir for the treatment of hospitalized 2019 coronavirus disease (COVID-19) patients, as described in the Scope of Authorization (section II) of this letter, pursuant to Section 564 of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[1] On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biologics during the COVID-19 outbreak, pursuant to section 564 of the Act, subject to terms of any authorization issued under that section.[2]

Remdesivir is a direct acting antiviral drug that inhibits viral RNA synthesis. It is an investigational drug and is not currently approved for any indication. Remdesivir has activity in cell culture and animal models against SARS-CoV, MERS-CoV, and SARS-CoV-2.

Based on review of the topline data from the randomized, double-blinded, placebo-controlled trial conducted by NIAID (NCT04280705) and from the Gilead-sponsored open-label trial that evaluated different durations of remdesivir (NCT04292899), it is reasonable to believe that the known and potential benefits of RDV outweigh the known and potential risks of the drug for the treatment of patients hospitalized with severe COVID-19.

Having concluded that the criteria for issuance of this authorization under 564(c) of the Act are met, I am authorizing the emergency use of remdesivir for treatment of COVID-19, as described

[1] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. February 4, 2020.*

[2] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of remdesivir for the treatment of COVID-19 when administered as described in the Scope of Authorization (section II) meet the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that remdesivir may be effective in treating COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of remdesivir when used to treat COVID-19 outweigh the known and potential risks of such products; and
3. There is no adequate, approved, and available alternative to the emergency use of remdesivir for the treatment of COVID-19.[3]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Distribution of the authorized remdesivir will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. Gilead will supply remdesivir to authorized distributors[4], or directly to a U.S. government agency, who will distribute to hospitals and other healthcare facilities as directed by the U.S. Government, in collaboration with state and local government authorities, as needed;

- The remdesivir covered by this authorization will be used only to treat adults and children with suspected or laboratory confirmed COVID-19 and severe disease defined as SpO2 ≤ 94% on room air, requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO);

- Remdesivir is administered in an in-patient hospital setting via intravenous (IV) infusion by a healthcare provider; and

[3] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.
[4] "Authorized Distributor(s)" are identified by Gilead as an entity or entities allowed to distribute authorized remdesivr.

- The use of remdesivir covered by this authorization should be in accordance with the dosing regimens as detailed in the authorized Facts Sheets.

Product Description

Remdesivir is a nucleoside ribonucleic acid (RNA) polymerase inhibitor. Remdesivir for injection, 100 mg, is a sterile, preservative-free lyophilized solid that is to be reconstituted with 19mL of sterile water for injection and diluted into 0.9% saline prior to intravenous (IV) administration. Following reconstitution, each single-dose, clear glass vial contains a 5 mg/mL remdesivir concentrated solution with sufficient volume to allow withdrawal of 20 mL. Remdesivir Injection, 5 mg/mL, is a sterile, preservative- free, clear, solution that is to diluted into 0.9% saline prior to intravenous (IV) administration. The authorized remdesivir vial label and/or the carton labeling is clearly marked for "emergency use authorization" or for "investigational use."[5]

Remdesivir for injection, 100 mg, vials should be stored below 30 °C until time of use. Remdesivir injection, 5 mg/mL vials should be stored at refrigerated temperatures (2 °C to 8 °C) until time of use. Following dilution with 0.9% saline, the solution can be stored for up to 4 hours at room temperature (20 °C to 25 °C) or 24 hours at refrigerated temperatures (2 °C to 8 °C).

Remdesivir is authorized to be accompanied by the following product-specific information pertaining to emergency use, which is required to be made available to healthcare providers and patients respectively:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Remdesivir (GS-5734)
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Remdesivir for Coronavirus Disease 2019 (COVID-19)

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of remdesivir when used for the treatment of COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that remdesivir may be effective for the treatment of COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that remdesivir (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

[5] The product labeled "investigational use" is authorized for use under this EUA; FDA is not requiring it to be relabeled given the immediate need for the product.

The emergency use of your product under an EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), remdesivir is authorized for the treatment of suspected or laboratory confirmed COVID-19 in adults and children who are hospitalized with severe disease as described in the Scope of Authorization (section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Gilead Sciences, Inc. (Gilead)

A. Gilead will ensure that the authorized remdesivir, accompanied with the authorized labeling (i.e., Fact Sheets), is distributed to hospitals and healthcare facilities as directed by the U.S. Government, consistent with the terms of this letter.

B. Gilead will ensure that appropriate storage and cold chain is maintained.

C. Gilead will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., U.S. government agencies, state and local government authorities, authorized distributors, healthcare facilities, healthcare providers) involved in distributing or receiving authorized remdesivir. Gilead will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (i.e., Fact Sheets).

D. Gilead may request changes to this authorization, including to the authorized Fact Sheets for remdesivir, and such changes may be permitted without amendment of this EUA, upon concurrence of the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research (CDER), the Counter-Terrorism and Emergency Coordination Staff/Office of Center Director/CDER, and Office of Counterterrorism Emerging Threats/Office Chief Scientist/Office of Commissioner.

E. Gilead will report to FDA serious adverse events and all medication errors associated with the use of the authorized remdesivir that are reported to Gilead during the pandemic using either of the following options.

   Option 1: Submit reports through the Safety Reporting Portal (SRP) as described on the FDA SRP web page.

   Option 2: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the FAERS electronic submissions web page.

Submitted reports under both options should state: "use of remdesivir was under an EUA". For reports submitted under Option 1, include this language at the beginning of the question "Describe Event" for further analysis. For reports submitted under Option 2, include this language at the beginning of the "Case Narrative" field.

F. Through a process of inventory control, Gilead will maintain records regarding distribution of the authorized remdesivir (i.e., lot numbers, quantity, receiving site, receipt date).

G. Gilead will make available to FDA upon request any records maintained in connection with this EUA.

Hospitals and Other Healthcare Facilities to Whom the Authorized Remdesivir Is Distributed and Healthcare Providers Administering the Authorized Remdesivir

H. Healthcare facilities and healthcare providers will ensure that they are aware of the letter of authorization, and the terms herein, and that the authorized Fact Sheets are made available to healthcare providers and to patients and caregivers, respectively, through appropriate means.

I. Healthcare facilities and healthcare providers receiving remdesivir will track serious adverse events that are considered to be potentially attributable to remdesivir use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit a MedWatch form (www.fda.gov/medwatch/report.htm), or Complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (these forms can be found via link above). Call 1-800-FDA-1088 for questions. Submitted reports should state, "use of remdesivir was under an EUA" at the beginning of the question "Describe Event" for further analysis.

J. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized remdesivir (i.e., lot numbers, quantity, receiving site, receipt date), product storage, and maintain patient information (e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered).

K. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Gilead and/or FDA. Such records will be made available to Gilead, HHS, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising and Promotion

L. All descriptive printed matter, including advertising and promotional material, relating to the use of the remdesivir shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

M. No descriptive printed matter, including advertising or promotional material, relating to the use of the remdesivir may represent or suggest that such products are safe or effective.

N. All descriptive printed matter, including advertising and promotional material, relating to the use of the remdesivir clearly and conspicuously shall state that:

- the remdesivir have not been approved;
- the remdesivir have been authorized by FDA under an EUA;
- the remdesivir is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the remdesivir under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

Denise M. Hinton -S3 Digitally signed by Denise M. Hinton -S3 Date: 2020.05.01 14:56:27 -04'00'

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures

May 8, 2020

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, IL 60047

Attention: Molly Ventrelli
Senior Vice President, Regulatory Affairs

Dear Ms. Ventrelli:

This letter is in response to your May 1, 2020, request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of Fresenius Propoven 2% Emulsion to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation in an Intensive Care Unit (ICU) setting during the 2019 coronavirus disease (COVID-19) pandemic, as described in the Scope of Authorization (Section II) of this letter, pursuant to Section 564 of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[1] On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biologics during the COVID-19 outbreak, pursuant to Section 564 of the Act, subject to terms of any authorization issued under that section.[2]

Fresenius Propoven 2% Emulsion is an intravenous (IV) sedative hypnotic drug that can be utilized to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting.

Based on published data from China and preliminary reports in the U.S., it has been noted that Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, has led to an increased population with critical illness, necessitating sedation drug products for mechanically ventilated patients. As a result, there is a shortage of FDA-approved propofol available for use in mechanically ventilated critically ill patients, as well as shortages of

[1] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. February 4, 2020.*

[2] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

alternative FDA-approved drugs, dexmedetomidine and midazolam, which are approved for sedation of mechanically ventilated patients in the ICU setting. Based on the totality of scientific evidence available, FDA has concluded that it is reasonable to believe that the Fresenius Propoven 2% Emulsion may be effective to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of your Fresenius Propoven 2% Emulsion, as described in the Scope of Authorization (Section II) of this letter, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Fresenius Propoven 2% Emulsion, as described in the Scope of Authorization (Section II) of this letter, to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation in an ICU setting, meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness requiring mechanical ventilation, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Fresenius Propoven 2% Emulsion may be effective to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19[3] who require mechanical ventilation in an ICU setting, and that, when used under the conditions described in this authorization, the known and potential benefits of Fresenius Propoven 2% Emulsion when used for the indication above outweigh the known and potential risks of such products; and
3. There is no adequate, approved, and available alternative to the emergency use of Fresenius Propoven 2% Emulsion due to shortages of FDA-approved alternatives during the COVID-19 pandemic.[4]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Fresenius Propoven 2% Emulsion will be used only to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation.

[3] In the circumstances of this public health emergency, it would not be feasible to require healthcare providers to seek to limit Fresenius Propoven 2% Emulsion only to be used for patients with suspected or confirmed COVID-19; therefore, this authorization does not limit use to such patients.

[4] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

- Fresenius Propoven 2% Emulsion will be administered only by a licensed healthcare provider in an ICU setting.
- Fresenius Propoven 2% Emulsion will not be administered to pregnant women, unless there are no FDA-approved products available to maintain sedation for these patients should they require mechanical ventilation in an ICU setting.
- Fresenius Propoven 2% Emulsion will be used only in accordance with the dosing regimens as detailed in the authorized Facts Sheets.

Product Description

Fresenius Propoven 2% Emulsion (propofol) is classified as a sedative hypnotic drug. It is an injectable emulsion containing 20 mg/mL of propofol for continuous IV administration to maintain sedation in patients greater than 16 years old who require mechanical ventilation in an ICU setting.

Fresenius Propoven 2% Emulsion is authorized to be accompanied by the following product-specific information pertaining to emergency use (referred to as "authorized labeling"), which is required to be made available to healthcare providers and patients respectively:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Fresenius Propoven 2% Emulsion
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Fresenius Propoven 2% Emulsion
- Diprivan and Fresenius Propoven 2% Emulsion Comparison Wall Chart
- Fresenius Propoven 2% Emulsion Advisory Stickers on double strength concentration for application to vial cap ("Advisory Stickers")

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Fresenius Propoven 2% Emulsion, when used to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting when used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Fresenius Propoven 2% Emulsion may be effective to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19 who require mechanical ventilation in an ICU setting when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Fresenius Propoven 2% Emulsion (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under an EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the

Conditions of Authorization (Section IV). Subject to the terms of an EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Fresenius Propoven 2% Emulsion is authorized to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19[5] who require mechanical ventilation in an ICU setting as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Fresenius Kabi USA, LLC

A. Fresenius Kabi USA, LLC may request changes to the authorized labeling as described in the Scope of Authorization (Section II) of this letter. Such requests will be made in consultation with, and require concurrence of, the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAMPM)/Office of Neuroscience (ON)/Office of New Drugs (OND)/Center for Drug Evaluation and Research (CDER), as appropriate.

B. Fresenius Kabi USA, LLC may request changes to the Scope of Authorization (Section II in this letter) of the product. Such requests will be made in consultation with, and require concurrence of, the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and DAAMPM/ON/OND/CDER.

C. Fresenius Kabi USA, LLC will manufacture Fresenius Propoven 2% Emulsion in conformance with CGMPs and all appropriate specifications.

D. Fresenius Kabi USA, LLC will perform and document process validation for Fresenius Propoven 2% Emulsion in 100 mL vials concurrently with the first manufactured batches. Additionally, Fresenius Kabi USA, LLC will add at least three representative lots of Fresenius Propoven 2% Emulsion to the firm's stability program.

E. Fresenius Kabi USA, LLC will report to FDA serious adverse events and all medication errors associated with the use of the Fresenius Propoven 2% Emulsion of which they become aware during the pandemic, to the extent practicable given emergency circumstances, using either of the following options.

   Option 1: Submit reports through the Safety Reporting Portal (SRP) as described on the FDA SRP web page.

[5] See footnote 3.

Option 2: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the FAERS electronic submissions web page.

Submitted reports under both options should state: "use of Fresenius Propoven 2% Emulsion was under an EUA". For reports submitted under Option 1, include this language at the beginning of the question "Describe Event" for further analysis. For reports submitted under Option 2, include this language at the beginning of the "Case Narrative" field.

Fresenius Kabi US, LLC and Authorized Distributors[6]

F. Fresenius Kabi USA, LLC will notify FDA of any authorized distributor(s) of the product, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA.

G. Fresenius Kabi USA, LLC and authorized distributor(s) will make Fresenius Propoven 2% Emulsion available with the authorized labeling as described in the Scope of Authorization (Section II) of this letter.

H. Fresenius Kabi USA, LLC and authorized distributor(s) will make available on their website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients and Parent/Caregivers.

I. Through a process of inventory control, Fresenius Kabi USA, LLC and authorized distributor(s) will maintain records of the healthcare settings to which they distribute Fresenius Propoven 2% Emulsion and the number of Fresenius Propoven 2% Emulsion they distribute.

J. Fresenius Kabi USA, LLC and authorized distributor(s) will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

K. Fresenius Kabi USA, LLC and authorized distributor(s) are authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.

Hospitals and Other Healthcare Facilities to Whom the Authorized Fresenius Propoven 2% Emulsion Is Distributed and Healthcare Providers Administering the Authorized Fresenius Propoven 2% Emulsion

L. Healthcare facilities and healthcare providers will ensure that they are aware of the letter of authorization, and the terms herein, and that the authorized labeling (as described in the Scope of Authorization (Section II) of this letter) is made available to healthcare providers and to patients and caregivers through appropriate means.

[6] "Authorized Distributor(s)" are identified by the sponsor in EUA requests as an entity allowed to distribute the product.

M. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized Fresenius Propoven 2% Emulsion (i.e., lot numbers, quantity, receiving site, receipt date), product storage, and maintain patient information (e.g., patient name, age, disease manifestation, days of infusion per patient, other drugs administered).

N. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Fresenius Kabi USA, LLC and/or FDA. Such records will be made available to Fresenius USA, LLC, HHS, and FDA for inspection upon request.

O. Healthcare facilities and prescribing health care providers or their designee receiving Fresenius Propoven 2% Emulsion will track all medication errors associated with the use of and all serious adverse events that are considered to be potentially attributable to Fresenius Propoven 2% Emulsion use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers using one of the following methods:

Option 1: Complete and submit a MedWatch form online (www.fda.gov/medwatch/report.htm)

Option 2: Complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (this form can be found via link above).

Call 1-800-FDA-1088 for questions. Submitted reports should state, "use of Fresenius Propoven 2% Emulsion was under an EUA" at the beginning of the question "Describe Event" for further analysis.

Conditions Related to Printed Matter, Advertising and Promotion

P. All descriptive printed matter, including advertising and promotional material, relating to the use of the Fresenius Propoven 2% Emulsion shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

Q. No descriptive printed matter, including advertising or promotional material, relating to the use of the Fresenius Propoven 2% Emulsion may represent or suggest that such products are safe or effective.

R. Except for the Advisory Stickers described in Section II, all descriptive printed matter, including advertising and promotional material, relating to the use of Fresenius Propoven 2% Emulsion clearly and conspicuously shall state that:

- the Fresenius Propoven 2% Emulsion is not FDA-approved;
- the Fresenius Propoven 2% Emulsion has been authorized by FDA for use under an EUA;

- the Fresenius Propoven 2% Emulsion is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

--/S/--

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures

June 15, 2020

Gary L. Disbrow Ph.D.
Deputy Assistant Secretary
Director, Medical Countermeasure Programs
Biomedical Advanced Research and Development Authority (BARDA)
Office of Assistant Secretary for Preparedness and Response (ASPR)
U.S. Department of Health and Human Services (HHS)
330 Independence Ave, S.W., Room 640G
Washington, D.C. 20201

Dear Dr. Disbrow:

This letter is in response to your request, dated today, that the Food and Drug Administration (FDA) revoke the Emergency Use Authorization (EUA) for emergency use of oral formulations of chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ) to be distributed from the Strategic National Stockpile (SNS) issued on March 28, 2020. Like BARDA's earlier request to FDA to issue the EUA, BARDA's request to revoke the EUA is part of a collaborative, USG-interagency effort to rapidly respond to this continuously evolving public health emergency. Today's request to revoke is based on new information, including clinical trial data results, that have led BARDA to conclude that this drug may not be effective to treat COVID-19 [Coronavirus Disease 2019] and that the drug's potential benefits for such use do not outweigh its known and potential risks.

The authorization of a product for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3) may, pursuant to section 564(g)(2) of the Act, be revised or revoked when the criteria under section 564(b)(1) of the Act no longer exist, the criteria under section 564(c) of the Act for issuance of such authorization are no longer met, or other circumstances make such revision or revocation appropriate to protect the public health or safety.

FDA has determined that the criteria under section 564(c) of the Act for issuance of the EUA referenced above are no longer met. Under section 564(c)(2) of the Act, an EUA may be issued only if FDA concludes "that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that: (A) the product may be effective in diagnosing, treating, or preventing—(i) such disease or condition [....]; and (B) the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product [...]."

As explained in the attached memorandum, based on a review of new information and a reevaluation of information available at the time the EUA was issued, FDA now concludes that these criteria are no longer met. The bases for this decision include the following:

Page 2 – BARDA

- We now believe that the suggested dosing regimens for CQ and HCQ as detailed in the Fact Sheets are unlikely to produce an antiviral effect.
- Earlier observations of decreased viral shedding with HCQ or CQ treatment have not been consistently replicated and recent data from a randomized controlled trial assessing probability of negative conversion showed no difference between HCQ and standard of care alone.
- Current U.S. treatment guidelines do not recommend the use of CQ or HCQ in hospitalized patients with COVID-19 outside of a clinical trial, and the NIH guidelines now recommend against such use outside of a clinical trial.
- Recent data from a large randomized controlled trial showed no evidence of benefit for mortality or other outcomes such as hospital length of stay or need for mechanical ventilation of HCQ treatment in hospitalized patients with COVID-19.

FDA has concluded that, based on this new information and other information discussed in the attached memorandum, it is no longer reasonable to believe that oral formulations of HCQ and CQ may be effective in treating COVID-19, nor is it reasonable to believe that the known and potential benefits of these products outweigh their known and potential risks. Accordingly, FDA revokes the EUA for emergency use of HCQ and CQ to treat COVID-19, pursuant to section 564(g)(2) of the Act. As of the date of this letter, the oral formulations of HCQ and CQ are no longer authorized by FDA to treat COVID-19.

While HCQ that has been distributed from SNS is no longer authorized under the EUA for the authorized use to treat hospitalized patients for COVID-19, FDA-approved HCQ can be distributed in interstate commerce. The CQ products covered by the EUA are not approved by FDA for any indication and therefore cannot be legally introduced into interstate commerce. In addition, under section 564(f)(2) of the Act, HCQ and CQ that were distributed from the SNS under this EUA remain authorized for emergency use to continue to treat any hospitalized patient to whom the authorized product has already been administered during the COVID-19 public health emergency, to the extent found necessary by such patient's attending physician.

Notice of this revocation will be published in the *Federal Register*, pursuant to section 564(h)(1) of the Act.

Sincerely,

/s/

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Dated: September 3, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020–20041 Filed 9–10–20; 8:45 am]

BILLING CODE 4164–01–C

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended, notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel; Review of Institutional Training Grants in Digestive Diseases and Nutrition.

Date: September 30, 2020.

Time: 9:00 a.m. to 6:00 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892 (Video Meeting).

Contact Person: Tian, Lan, Ph.D., Scientific Review Officer, Review Branch, DEA, NIDDK, National Institutes of Health, Suite 7016, 6707 Democracy Boulevard, Bethesda, MD 20892–5452, (301) 496–7050, *tianl@niddk.nih.gov.*

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases