3. *The date the application was approved:* November 20, 2019. FDA has verified the applicant's claim that NDA 212194 was approved on November 20, 2019.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the USPTO applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 190 days of patent term extension.

III. Petitions

Anyone with knowledge that any of the dates as published are incorrect may submit either electronic or written comments and, under 21 CFR 60.24, ask for a redetermination (see **DATES**). Furthermore, as specified in § 60.30 (21 CFR 60.30), any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period. To meet its burden, the petition must comply with all the requirements of § 60.30, including but not limited to: must be timely (see **DATES**), must be filed in accordance with § 10.20, must contain sufficient facts to merit an FDA investigation, and must certify that a 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: June 16, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–13176 Filed 6–22–21; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–N–1729]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of an Emergency Use Authorization (EUA) (the Authorization) for a drug for use during the COVID–19 pandemic. FDA issued the Authorization under the Federal Food, Drug, and Cosmetic Act (FD&C Act), as requested by B. Braun Melsungen AG. The Authorization contains, among other things, conditions on the emergency use of the authorized drug. The Authorization follows 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 United States 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 revocation of the Authorization issued to Eli Lilly and Company for bamlanivimab alone. FDA revoked this authorization on April 16, 2021. Reprinted in this document is the issuance of the Authorization and the revocation, which include an explanation of the reasons for issuance or revocation.

DATES: The Authorization for B. Braun Melsungen AG was effective as of March 12, 2021 and the revocation for Eli Lilly and Company was effective as of April 16, 2021.

ADDRESSES: Submit written requests for single copies of the Authorization and/or revocation 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.

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 United States (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

[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.

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 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 Authorization

The Authorization follows 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 United States 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 authorized the emergency use of a drug during the COVID–19 pandemic. On March 12, 2021, FDA issued an EUA to B. Braun Melsungen AG for Propofol-Lipuro 1% injectable emulsion, subject to the terms of the Authorization. The Authorization in its entirety (not including the authorized version of the fact sheets and other written materials) follows, below in section VI Electronic Access, and provides 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

On November 9, 2020, FDA issued an Authorization to Eli Lilly and Company for bamlanivimab alone and reissued the Authorization on February 9, 2021 and March 2, 2021. Notice of the issuance of the Authorization was published in the **Federal Register** on February 19, 2021 (86 FR 10290), as required by section 564(h)(1) of the FD&C Act. FDA authorized bamlanivimab alone for emergency use for the treatment of mild to moderate COVID–19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS–CoV–2 viral testing, and who are at high risk for progressing to severe Coronavirus Disease 2019 (COVID–19) and/or hospitalization. Subsequent to the issuance of the Authorization, as described in the revocation letter reprinted in this notice, FDA considered new data and new information that became available. 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 April 16, 2021, FDA revoked the EUA for Eli Lilly and Company for bamlanivimab alone because the criteria for issuance were no longer met. Based on a review of the new data and new information, FDA concluded it is no longer reasonable to believe that the known and potential benefits of bamlanivimab alone outweigh the known and potential risks for the product. A summary of these new data and new information includes the following:

- Vesicular stomatitis virus-based pseudovirus expressing spike protein with variant substitutions, specifically E484K and L452R, exhibit large reductions (>1,000 fold) in susceptibility to bamlanivimab alone in neutralization assays.
- The Centers for Disease Control and Prevention (CDC) national genomic surveillance program has reported an increasing frequency of SARS–CoV–2 variants that are expected to be resistant to bamlanivimab alone.
- Testing technologies that enable health care providers to test individual patients for SARS–CoV–2 viral variants prior to initiation of treatment with monoclonal antibodies are not available and frequencies are changing rapidly. Therefore, empiric treatment with monoclonal antibody therapies that are expected to retain activity broadly across the U.S. is needed to reduce the likelihood of treatment failure.
- On April 8, 2021, the National Institutes of Health updated its treatment guidelines for COVID–19 recommending against the use of bamlanivimab alone.

Accordingly, FDA revoked the EUA for emergency use of bamlanivimab alone 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 Eli Lilly and Company for bamlanivimab alone.

[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.

The revocation in its entirety follows, below in 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 Authorization and revocation are available on the internet from *https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.*

BILLING CODE 4164–01–P

March 12, 2021

B. Braun Melsungen AG
Attention: Rebecca Stolarick
Registered Agent
901 Marcon Boulevard
Allentown, PA 18109

RE: Emergency Use Authorization 096

Dear Ms. Stolarick:

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 Propofol-Lipuro 1% injectable emulsion for infusion 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 biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act, subject to terms of any authorization issued under that section.[2]

Propofol-Lipuro 1% injectable emulsion for infusion 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.

The Agency has 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,

[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).

necessitating sedation drug products for mechanically ventilated patients. As a result, there is an insufficient supply of the FDA-approved propofol available for use in mechanically ventilated critically ill patients.[3] Based on the totality of scientific evidence available, FDA has concluded that it is reasonable to believe that the Propofol-Lipuro 1% injectable emulsion for infusion 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 Propofol-Lipuro 1% injectable emulsion for infusion, 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 Propofol-Lipuro 1% injectable emulsion for infusion, as described in the Scope of Authorization (Section II) of this letter, 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 Propofol-Lipuro 1% injectable emulsion for infusion may be effective to maintain sedation via continuous infusion in patients greater than 16 years old with suspected or confirmed COVID-19[4] who require mechanical ventilation in an ICU setting, and that, when administered as described in the Scope of Authorization (Section II) and used under the conditions described in this authorization, the known and potential benefits of Propofol-Lipuro 1% injectable emulsion for infusion outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of Propofol-Lipuro 1% injectable emulsion for infusion due to insufficient supplies of FDA-approved alternatives to fully meet the emergency need during the COVID-19 pandemic.[5]

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[3] FDA also assessed the supply of FDA-approved alternatives, which includes dexmedetomidine and midazolam. At the time of this authorization, FDA has determined that there is insufficient supply of the FDA-approved alternatives to fully meet the emergency need for Propofol-Lipuro 1% injectable emulsion for infusion in 100 mL vials.

[4] In the circumstances of this public health emergency, it would not be feasible to require healthcare providers to seek to limit Propofol-Lipuro 1% injectable emulsion for infusion only to be used for patients with suspected or confirmed COVID-19; therefore, this authorization does not limit use to such patients.

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

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:

- Propofol-Lipuro 1% injectable emulsion for infusion will be used only to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation.[6]
- Propofol-Lipuro 1% injectable emulsion for infusion will be administered only by a licensed healthcare provider in an ICU setting.
- Propofol-Lipuro 1% injectable emulsion for infusion 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.
- Propofol-Lipuro 1% injectable emulsion for infusion will be used only in accordance with the dosing regimens as detailed in the authorized Facts Sheets.

Product Description

Propofol-Lipuro 1% injectable emulsion for infusion is classified as a sedative hypnotic drug. The authorized product is an injectable emulsion in 100 mL vials containing 10 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.

Propofol-Lipuro 1% injectable emulsion for infusion is authorized for emergency use as described in the Scope of Authorization (Section II) with the following product-specific information to be made available to healthcare providers and patients, parents and caregivers, respectively, through B. Braun Melsungen's website at: https://www.bbraunusa.com/en/company/newsroom/covid19.html#,

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Propofol-Lipuro 1% injectable emulsion for infusion
- Fact Sheet for Patients, Parents, and Caregivers: Emergency Use Authorization (EUA) of Propofol-Lipuro 1% injectable emulsion for infusion

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 Propofol-Lipuro 1% injectable emulsion for infusion, 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 Propofol-Lipuro 1% injectable

[6] See footnote 4.

emulsion for infusion may be effective 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 Propofol-Lipuro 1% injectable emulsion for infusion (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), Propofol-Lipuro 1% injectable emulsion for infusion is authorized 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 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:

B. Braun Melsungen and Authorized Distributors[7]

A. B. Braun Melsungen and authorized distributor(s) will ensure that the authorized Propofol-Lipuro 1% injectable emulsion is distributed and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and healthcare providers consistent with the terms of this letter.

B. B. Braun Melsungen and authorized distributor(s) will ensure appropriate storage is maintained until the product is delivered to healthcare facilities and/or healthcare providers.

C. B. Braun Melsungen authorized distributor(s) 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 Propofol-Lipuro 1% injectable emulsion for infusion. B. Braun Melsungen 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).

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

D. B. Braun Melsungen may request changes to this authorization, including to the authorized Fact Sheets for Propofol-Lipuro 1% injectable emulsion for infusion. Any request for changes to this EUA must be submitted to the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)/Office of Neuroscience/Office of New Drugs/Center for Drug Evaluation and Research (CDER). Such changes require appropriate authorization from FDA prior to implementation.[8]

E. B. Braun Melsungen may develop and disseminate instructional and educational materials (e.g., materials providing information on product administration and/or patient monitoring) that are consistent with the authorized emergency use of Propofol-Lipuro 1% injectable emulsion for infusion as described in this letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs. Any instructional and educational materials that are inconsistent with the authorized labeling of Propofol-Lipuro 1% injectable emulsion for infusion are prohibited. Should the Agency become aware of any instructional or educational materials that are inconsistent with the authorized labeling of Propofol-Lipuro injectable emulsion for infusion, the Agency will require B. Melsungen to cease distribution of such instructional or educational materials.

F. B. Braun Melsungen will report to FDA serious adverse events and all medication errors associated with the use of the Propofol-Lipuro 1% injectable emulsion for infusion that are reported to B. Braun Melsungen 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: "Propofol-Lipuro 1% use for COVID-19 under Emergency Use Authorization (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.

[8] The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study; (8) new strengths of the authorized product, new product sources (e.g., of active pharmaceutical ingredient) or of product components. All changes to the authorization require review and concurrence from DAAP/CDER. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), (7), or (8), review and concurrence also is required from the Counter-Terrorism and Emergency Coordination Staff/Office of the Center Director/CDER and the Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist.

G. All manufacturing, packaging, and testing sites for both drug substance and drug product will comply with current good manufacturing practice requirements of Section 501(a)(2)(B) of the Act.

H. B. Braun Melsungen will submit information to the Agency within three working days of receipt concerning significant quality problems with distributed drug product of Propofol-Lipuro 1%, that includes the following: (i) Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or (ii) Information concerning any microbiological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug product, or any failure of one or more distributed batches of the drug product to meet established specifications. If a quality problem affects unreleased product and may also implicate product(s) previously released and distributed, then the quality alert should be submitted for all impacted lots. B. Braun Melsungen will include in its notification to the Agency whether the batch, or batches, in question will be recalled. If FDA requests that these, or any other batches, at any time, be recalled, B. Braun Melsungen must recall them.

I. Braun Melsungen will manufacture Propofol-Lipuro 1% injectable emulsion for infusion to meet all quality standards, and per the manufacturing process and control strategy as detailed in B. Braun Melsungen's EUA request. B. Braun Melsungen will not implement any changes to the description of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and quality of the authorized product, without prior notification to and concurrence by the Agency as described in condition D.

J. B Braun Melsungen will list Propofol-Lipuro 1% injectable emulsion for infusion with a unique product NDC under the marketing category of Unapproved Drug- Other. Further, the listing will include each establishment where manufacturing is performed for the drug and the type of operation performed at each such establishment.

K. Through a process of inventory control, B. Braun Melsungen and authorized distributor(s) will maintain records distribution of the authorized product (i.e., lot numbers, quantity, receiving site, receipt date).

L. B. Braun Melsungen and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

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

M. 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, prior to administration of Propofol-Lipuro 1% injectable emulsion for infusion as described in the Scope of Authorization (Section II) under this EUA.

N. Healthcare facilities and healthcare providers receiving Propofol-Lipuro 1% injectable emulsion for infusion will track serious adverse events that are considered to be potentially attributable to the use of Propofol-Lipuro 1% injectable emulsion for infusion under this authorization 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, "Propofol-Lipuro 1% injectable emulsion for infusion use for COVID-19 under Emergency Use Authorization (EUA)" at the beginning of the question "Describe Event" for further analysis.

O. Healthcare facilities and healthcare providers will ensure that appropriate storage is maintained until the products are administered consistent with the terms of this letter.

P. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized Propofol-Lipuro 1% injectable emulsion for infusion (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).

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

Conditions Related to Printed Matter, Advertising and Promotion

R. All descriptive printed matter, as well as advertising and promotional material, relating to the use of the Propofol-Lipuro 1% injectable emulsion for infusion 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.

S. No descriptive printed matter, as well as advertising or promotional material, relating to the use of the Propofol-Lipuro 1% injectable emulsion for infusion may represent or suggest that such products are safe or effective.

T. All descriptive printed matter, as well as advertising and promotional material, relating to the use of Propofol-Lipuro 1% injectable emulsion for infusion clearly and conspicuously shall state that:

- the Propofol-Lipuro 1% injectable emulsion for infusion is not FDA-approved, but has been authorized for emergency use by FDA 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

- the Propofol-Lipuro 1% injectable emulsion for infusion 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

U.S. FOOD & DRUG ADMINISTRATION

April 16, 2021

Susan Warner, Pharm.D.
Advisor
Global Regulatory Affairs - US
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285

RE: Emergency Use Authorization 090

Dear Dr. Warner:

This letter is in response to your request, dated April 15, 2021, that the Food and Drug Administration (FDA) revoke the Emergency Use Authorization (EUA) for emergency use of bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe Coronavirus Disease 2019 (COVID-19) and/or hospitalization. The EUA (EUA 090) was originally issued on November 9, 2020 and reissued on February 9, 2021 and March 2, 2021.

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.

As part of the Agency's ongoing review of the circumstances and appropriateness of EUA 090, FDA has continually reviewed new data and additional new information to assess whether the criteria for issuance of EUA 090 continue to be met. Under section 564(c)(2) of the Act, an EUA may be issued only if FDA concludes, among other things, "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 [...]."

Since the initial authorization of bamlanivimab for emergency use, there has been a sustained increase in SARS-CoV-2 viral variants across the U.S. that are resistant to bamlanivimab administered alone. As part of the Agency's ongoing review of the circumstances and appropriateness of EUA 090, we reviewed emerging information and assessed whether, based on the totality of scientific evidence available, the criteria for issuance of the EUA continue to be met.

A summary of these new data and new information includes the following:

- Vesicular stomatitis virus-based pseudovirus expressing spike protein with variant substitutions, specifically E484K and L452R, exhibit large reductions (>1,000 fold) in susceptibility to bamlanivimab alone in neutralization assays.

- The Center for Disease Control (CDC) national genomic surveillance program has reported an increasing frequency of SARS-CoV-2 variants that are expected to be resistant to bamlanivimab alone.
    - As of mid-March 2021, approximately 20% of isolates sequenced in the U.S. were reported as lineages expected to be resistant to bamlanivimab alone, increasing from approximately 5% in mid-January 2021.
    - The CDC national genomic surveillance program has published detailed data regarding variants of the B.1.427 and B.1.429 lineages, first detected in California, which harbor the L452R substitution. These variants have now been identified at frequencies exceeding 20% in eight states and frequencies exceeding 10% in two additional states.
    - There are recent reports that variants with the E484K substitution are circulating at rates exceeding 10% in the New York City metropolitan area including northern New Jersey.

- Testing technologies that enable health care providers to test individual patients for SARS-CoV-2 viral variants prior to initiation of treatment with monoclonal antibodies are not available and frequencies are changing rapidly. Therefore, empiric treatment with monoclonal antibody therapies that are expected to retain activity broadly across the U.S. is needed to reduce the likelihood of treatment failure.

- On April 8, 2021, the National Institutes of Health updated its treatment guidelines for COVID-19 recommending against the use of bamlanivimab alone.

Given the above, we have concluded that the known and potential benefits of bamlanivimab alone no longer outweigh the known and potential risks for the product. As such, FDA has determined that the criteria under section 564(c) of the Act for issuance of EUA 090 referenced above are no longer met.

In your letter requesting that FDA revoke EUA 090, you state that you do not intend to request the return of bamlanivimab that has been distributed prior to this revocation, as the distributed product continues to be authorized for use together with etesevimab under EUA 094. FDA concurs with this approach toward disposition of the previously distributed bamlanivimab authorized for emergency use under EUA 090. Stakeholders may order etesevimab alone to pair with existing supply of bamlanivimab that may be on hand.

Accordingly, FDA revokes the EUA for emergency use of bamlanivimab administered alone for the treatment of mild to moderate COVID-19, pursuant to section 564(g)(2) of the Act.

Page 3 – Dr. Warner, Eli Lilly and Company

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: June 17, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–13183 Filed 6–22–21; 8:45 am]

BILLING CODE 4164–01–C

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA–2020–E–1256; FDA–2020–E–1257; and FDA–2020–E–1258]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or the Agency) has determined the regulatory review period for TURALIO and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of applications to the Director of the U.S. Patent and Trademark Office (USPTO), Department of Commerce, for the extension of a patent which claims that human drug product.

DATES: Anyone with knowledge that any of the dates as published (see the **SUPPLEMENTARY INFORMATION** section) are incorrect may submit either electronic or written comments and ask for a redetermination by August 23, 2021. Furthermore, any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period by December 20, 2021. See ''Petitions'' in the **SUPPLEMENTARY INFORMATION** section for more information.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before August 23, 2021. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of August 23, 2021. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket Nos. FDA–2020–E–1256; FDA–2020–E–1257; and FDA–2020–E–1258, for ''Determination of Regulatory Review Period for Purposes of Patent Extension; TURALIO.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management