DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2021–N–0335]

Authorizations of Emergency Use of Certain Biological Products 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 two Emergency Use Authorizations (EUAs) (the Authorizations) under the Federal Food, Drug, and Cosmetic Act (FD&C Act) for biological products for use during the COVID–19 pandemic. FDA has issued one Authorization for a biological product as requested by GlaxoSmithKline LLC and one Authorization for a biological product as requested by Genentech, Inc. The Authorizations contain, among other things, conditions on the emergency use of the authorized products. The Authorizations follow the February 4, 2020, determination by the Secretary of Health and Human Services (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, now named SARS–CoV–2, 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. The Authorizations, which include an explanation of the reasons for issuance, are reprinted in this document.

DATES: The Authorization for GlaxoSmithKline LLC is effective as of May 26, 2021, and the Authorization for Genentech, Inc. is effective as of June 24, 2021.

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. 4340, 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 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 (among other criteria).

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, U.S. Code, of attack with (A) a biological, chemical, radiological, or nuclear agent or agents; or (B) 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. Under section 564(h)(1) of the FD&C Act, revisions to an authorization shall be made available on the internet website of FDA. 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 in an actual or potential emergency 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

[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.

[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.

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, now named SARS–CoV–2, 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 two authorizations for the emergency use of biological products during the COVID–19 pandemic. On May 26, 2021, FDA issued an EUA to GlaxoSmithKline LLC for sotrovimab, subject to the terms of the Authorization. On June 24, 2021, FDA issued an EUA to Genentech, Inc. for ACTEMRA (tocilizumab), subject to the terms of the Authorization. The initial Authorizations, which are included below in their entirety after section IV of this document (not including the authorized versions of the fact sheets and other written materials), provide an explanation of the reasons for issuance, as required by section 564(h)(1) of the FD&C Act. Any subsequent reissuances of these Authorizations can be found on FDA's web page: *https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.*

IV. Electronic Access

An electronic version of this document and the full text of the Authorizations and 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

May 26, 2021

GlaxoSmithKline LLC
Attention: Debra H. Lake, M.S.
Senior Director, Global Regulatory Affairs
Five Moore Drive
PO Box 13398
Durham, North Carolina 27709

RE: Emergency Use Authorization 100

Dear Ms. Lake:

This letter is in response to GlaxoSmithKline LLC's (GSK) request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of sotrovimab for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19), 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 coronavirus disease 2019 (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 Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.[2]

Sotrovimab is a recombinant human IgG1κ monoclonal antibody that binds to a conserved epitope on the spike protein receptor binding domain of SARS-CoV-2. Sotrovimab does not compete with human ACE2 receptor binding. Sotrovimab is an investigational drug and is not currently approved for any indication.

Based on review of the interim analysis of phase 1/2/3 data from the COMET-ICE clinical trial (NCT #04545060), a randomized, double-blind, placebo-controlled clinical trial evaluating the safety and efficacy of sotrovimab 500 mg IV in outpatient (non-hospitalized) adults with SARS-CoV-2 infection, it is reasonable to believe that sotrovimab may be effective for the treatment 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).

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 progression to severe COVID-19, including hospitalization or death, and when used under the conditions described in this authorization, the known and potential benefits of sotrovimab outweigh the known and potential risks of such product.

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 sotrovimab for treatment of COVID-19, as described 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 sotrovimab for the treatment of COVID-19 when administered as described in the Scope of Authorization (Section II) meets 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 sotrovimab may be effective in treating 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 progression to severe COVID-19, including hospitalization or death, and that, when used under the conditions described in this authorization, the known and potential benefits of sotrovimab outweigh the known and potential risks of such products; and

3. There is no adequate, approved, and available alternative to the emergency use of sotrovimab 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 progression to severe COVID-19, including hospitalization or death.[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:

- Sotrovimab will be used only by healthcare providers to treat 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 progression to severe COVID-19, including hospitalization or death;

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

- Sotrovimab is not authorized for use in the following patient populations[4]:
    - Adults or pediatric patients who are hospitalized due to COVID-19, or
    - Adults or pediatric patients who require oxygen therapy due to COVID-19, or
    - Adults or pediatric patients who require an increase in baseline oxygen flow rate due to COVID-19 in those patients on chronic oxygen therapy due to underlying non-COVID-19-related comorbidity.

- Sotrovimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

- The use of sotrovimab covered by this authorization must be in accordance with the authorized Fact Sheets.

Product Description

Sotrovimab is supplied in individual single dose vials. Individual vials and carton container labeling for sotrovimab are clearly marked "For use under Emergency Use Authorization." Sotrovimab is a recombinant human IgG1κ monoclonal antibody that binds to a conserved epitope on the spike protein receptor binding domain of SARS-CoV-2. Sotrovimab does not compete with human ACE2 receptor binding.

Sotrovimab is available as a 500 mg/8 mL (62.5 mg/mL) sterile, preservative-free, clear, colorless or yellow to brown solution to be diluted prior to infusion. Unopened vials of sotrovimab should be stored under refrigerated temperature at 2°C to 8°C (36°F to 46°F). The vials should be kept in the individual original cartons to protect from light. The diluted infusion solution of sotrovimab should be administered immediately. If immediate administration is not possible, store the diluted infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) including transportation and infusion time.

Each carton containing a single treatment course of the authorized sotrovimab will include a single copy each of the following product-specific documents detailing information pertaining to its emergency use (referred to as "authorized labeling")[5]:

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) of sotrovimab

- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of sotrovimab for the treatment Coronavirus Disease 2019 (COVID-19)

[4] Benefit of treatment with sotrovimab has not been observed in patients hospitalized due to COVID-19. SARS-CoV-2 monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID 19 requiring high flow oxygen or mechanical ventilation.

[5] The authorized labeling for EUA 100 will also be available on GSK's website at www.sotrovimab.com

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 sotrovimab, when used for the treatment of COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh the 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 sotrovimab 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 sotrovimab (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 III). 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), sotrovimab is authorized to treat mild-to-moderate COVID-19 illness 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, who are at high risk for progression to severe COVID-19, including hospitalization or death, 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:

GSK and Authorized Distributors[6]

A. GSK and authorized distributor(s) will ensure that the authorized labeling (i.e., Fact Sheets) will accompany the authorized sotrovimab as described in Section II of this Letter of Authorization.

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

C. GSK and 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 sotrovimab. GSK will provide to all relevant stakeholders a copy of this letter of authorization and communicate any

[6] "Authorized Distributor(s)" are identified by GSK as an entity or entities allowed to distribute authorized sotrovimab.

subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (i.e., Fact Sheets).

D. GSK may request changes to this authorization, including to the authorized Fact Sheets for sotrovimab. Any request for changes to this EUA must be submitted to the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research. Such changes require appropriate authorization prior to implementation.[7]

E. GSK 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 sotrovimab 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 for sotrovimab are prohibited. If the Agency notifies GSK that any instructional and educational materials are inconsistent with the authorized labeling, GSK must cease distribution of such instructional and educational materials in accordance with the Agency's notification. Furthermore, as part of its notification, the Agency may also require GSK to issue corrective communication(s).

F. GSK will report to FDA serious adverse events and all medication errors associated with the use of the authorized sotrovimab that are reported to GSK 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: "Sotrovimab 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.

[7] 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. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), (7), or (8), review and concurrence 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 the FD&C Act section 501(a)(2)(B).

H. GSK will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with distributed drug product of sotrovimab that includes the following:

- Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or
- 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 product to meet the established specifications.

If a significant quality problem affects unreleased product and may also impact product(s) previously released and distributed, then information should be submitted for all potentially impacted lots.

GSK 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, GSK must recall them.

If not included in its initial notification, GSK must submit information confirming that GSK has identified the root cause of the significant quality problems, taken corrective action, and provide a justification confirming that the corrective action is appropriate and effective. GSK must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

I. GSK will manufacture sotrovimab to meet all quality standards and per the manufacturing process and control strategy as detailed in GSK's EUA request. GSK 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 notification to and concurrence by the Agency as described under condition D.

J. GSK will list sotrovimab with a unique 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 such establishment.

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

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

M. GSK will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2. A summary of GSK's process should be submitted to the Agency as soon as practicable, but no later than 30 calendar days of the issuance of this letter, and within 30 calendar days of any material changes to such process. GSK will provide reports to the Agency on a monthly basis summarizing any findings as a result of its monitoring activities and, as needed, any follow-up assessments planned or conducted.

N. FDA may require GSK to assess the activity of the authorized sotrovimab against any global SARS-CoV-2 variant(s) of interest (e.g., variants that are prevalent or becoming prevalent that harbor substitutions in the target protein or in protein(s) that interact with the target protein). GSK will perform the required assessment in a manner and timeframe agreed upon by GSK and the Agency. GSK will submit to FDA a preliminary summary report immediately upon completion of its assessment followed by a detailed study report within 30 calendar days of study completion. GSK will submit any relevant proposal(s) to revise the authorized labeling based on the results of its assessment, as may be necessary or appropriate based on the foregoing assessment.

O. GSK shall provide samples as requested of the authorized sotrovimab to the U.S. Department of Health and Human Services (HHS) for evaluation of activity against emerging global viral variants of SARS-CoV-2, including specific amino acid substitution(s) of interest (e.g., variants that are highly prevalent or that harbor substitutions in the target protein) within 5 business days of any request made by HHS. Analyses performed with the supplied quantity of authorized sotrovimab may include, but are not limited to, cell culture potency assays, protein binding assays, cell culture variant assays (pseudotyped virus-like particles and/or authentic virus), and *in vivo* efficacy assays.

P. GSK will submit to FDA all sequencing data assessing sotrovimab, including sequencing of any participant samples from the full analysis population from COMET-ICE that have not yet been completed no later than September 30, 2021. GSK will provide the Agency with a frequency table reporting all substitutions detected for all participants at all available timepoints at a frequency >1%.

Q. GSK will submit to FDA all SARS-CoV-2 viral shedding and viral load data, including quantitation of viral shedding and viral load for any participant samples from the full analysis population from COMET-ICE that have not yet been completed, no later than June 30, 2021.

<u>Healthcare Facilities to Whom the Authorized Sotrovimab Is Distributed and Healthcare Providers Administering the Authorized Sotrovimab</u>

R. 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 sotrovimab.

S. Healthcare facilities and healthcare providers receiving sotrovimab will track serious adverse events that are considered to be potentially attributable to sotrovimab 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, "Sotrovimab use for COVID-19 under Emergency Use Authorization" at the beginning of the question "Describe Event" for further analysis.

T. Healthcare facilities and healthcare providers will ensure that appropriate storage and cold chain is maintained until the product is administered consistent with the terms of this letter.

U. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized sotrovimab (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).

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

Conditions Related to Printed Matter, Advertising and Promotion

W. All descriptive printed matter, advertising, and promotional materials relating to the use of the sotrovimab under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in section 502(a) and (n) of the Act and FDA implementing regulations. In addition, such materials shall:

- Be tailored to the intended audience.
- Not take the form of reminder advertisements, as that term is described in 21 CFR 202.1(e)(2)(i), 21 CFR 200.200 and 21 CFR 201.100(f).
- Present risk information concurrently in the audio and visual parts of the presentation for advertisements disseminated through media such as radio, television, or telephone communications.
- Be accompanied by the authorized labeling.
- Be submitted to FDA accompanied by Form FDA-2253 at the time of initial dissemination or first use.

If the Agency notifies GSK that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions W-Y of this EUA, GSK must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency's notification. Furthermore, as part of its notification, the Agency may also require GSK to issue corrective communication(s).

X. No descriptive printed matter, advertising, or promotional materials relating to the use of sotrovimab under this authorization may represent or suggest that sotrovimab is safe or effective when used 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 progression to severe COVID-19, including hospitalization or death.

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

- Sotrovimab has not been approved, but has been authorized for emergency use by FDA under an EUA, to treat 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 progression to severe COVID-19, including hospitalization or death; and

- The emergency use of sotrovimab is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization 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 biological products during the COVID-19 pandemic 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

June 24, 2021

Hoffmann-La Roche, Ltd.
C/O Genentech, Inc.
Attention: Dhushy Thambipillai
Regulatory Project Management
1 DNA Way, Bldg 45-1
South San Francisco, CA 94080

RE: Emergency Use Authorization 099

Dear Ms. Thambipillai:

This letter is in response to Genentech, Inc.'s (Genentech) request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of Actemra[1] (tocilizumab) for the treatment of coronavirus disease 2019 (COVID-19) in certain hospitalized 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 coronavirus disease 2019 (COVID-19).[2] 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 (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.[3]

Actemra is a recombinant humanized monoclonal antibody that selectively binds to both soluble and membrane-bound human IL-6 receptors (sIL-6R and mIL-6R) and subsequently inhibits IL-6-mediated signaling through these receptors. Actemra is FDA-approved for several indications[4]; however, Actemra is not approved for the treatment of COVID-19.

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[1] For the purposes of this Letter of Authorization, the use of the tradename, Actemra, is intended to refer to the commercially available Actemra that is in United States distribution under the approved Biologics License Application 125276, only. As discussed further in Section II of this letter, Actemra that is commercially available under this licensure is authorized for emergency use consistent with the terms and conditions of this letter.

[2] 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.

[3] 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).

[4] The currently approved labeling for Actemra may be found at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125472s044lbl.pdf.

Based on review of the data from the RECOVERY clinical trial (NCT #04381936), a randomized, open-label, controlled, platform trial; the COVACTA clinical trial (NCT #04320615), a randomized, double-blind, placebo-controlled clinical trial; the EMPACTA clinical trial (NCT #04372186), a randomized, double-blind, placebo-controlled clinical trial; and the REMDACTA clinical trial (NCT #04409262), a randomized, double-blind, placebo-controlled clinical trial, it is reasonable to believe that Actemra may be effective for the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO), and when used under the conditions described in this authorization, the known and potential benefits of Actemra outweigh the known and potential risks of such product.

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 Actemra for the treatment of COVID-19, as described 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 Actemra for the treatment of COVID-19 when administered as described in the Scope of Authorization (Section II) meets 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 Actemra may be effective for the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO, and that, when used under the conditions described in this authorization, the known and potential benefits of Actemra outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative to the emergency use of Actemra for the treatment of COVID-19 in hospitalized adults and pediatric patients (2

years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.[5,6]

II. Scope of Authorization

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

- Actemra will be used only by healthcare providers to treat COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.
- Actemra may only be administered via intravenous infusion.
- The use of Actemra covered by this authorization must be in accordance with the authorized Fact Sheets.

Product Description

Actemra is supplied in individual single dose vials. Actemra is a recombinant humanized monoclonal antibody that selectively binds to both soluble and membrane-bound human IL-6 receptors (sIL-6R and mIL-6R) and subsequently inhibits IL-6-mediated signaling through these receptors.

Actemra injection is a preservative-free, sterile clear, colorless to pale yellow solution. The authorized product includes commercially available[7] Actemra, which is supplied as 80 mg/4 mL (NDC 50242-135-01), 200 mg/10 mL (NDC 50242-136-01), and 400 mg/20 mL (NDC 50242-137-01) individually packaged 20 mg/mL single-dose vials for further dilution prior to intravenous infusion. Do not use beyond the expiration date on the container or package. Actemra must be refrigerated at 36°F to 46°F (2°C to 8°C). Do not freeze. Protect the vials from light by storage in the original package until time of use.

[5] On October 22, 2020, Veklury (remdesivir) was approved to treat COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization. Veklury is a nucleoside ribonucleic acid polymerase inhibitor that has demonstrated antiviral activity against SARS-COV-2. Actemra is a recombinant humanized monoclonal antibody that selectively binds to both soluble and membrane-bound human IL-6 receptors (sIL-6R and mIL-6R) and subsequently inhibits IL-6-mediated signaling through these receptors. Severe COVID-19 infection has been associated with hyperinflammation. In this context, high levels of IL-6, as well as other pro-inflammatory cytokines and inflammatory markers, have been observed in some patients with severe COVID-19 infection. Thus, a product inhibiting IL-6, such as Actemra, may potentially act on the COVID-19-associated inflammatory response. This is distinct from Veklury, which acts as an antiviral agent. We also note that Veklury's FDA-approved indication is for a narrower population than the use authorized for Actemra under this EUA.
[6] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.
[7] Supra at Note 1.

Actemra is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and patients, parents, and caregivers, respectively, through Genentech's website at www.actemrahcp.com/covid-19 (referred to as the "authorized labeling"):

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) for Actemra
- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of Actemra 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 Actemra, when used for the treatment of COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh the 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 Actemra 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 Actemra (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.

III. Conditions of Authorization

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

Genentech and Authorized Distributors[8]

A. Genentech and authorized distributor(s) will ensure that Actemra is distributed with the FDA-approved package insert and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers as described in Section II of this Letter of Authorization.

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

C. Genentech and 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 Actemra. Genentech will provide to all relevant

[8] "Authorized Distributor(s)" are identified by Genentech as an entity or entities allowed to distribute Actemra for the use authorized in this letter.

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. Genentech may request changes to this authorization, including to the authorized Fact Sheets for Actemra. Any request for changes to this EUA must be submitted to the Division of Pulmonology, Allergy and Critical Care/Office of Immunology and Inflammation/Office of New Drugs/Center for Drug Evaluation and Research (CDER). Such changes require appropriate authorization prior to implementation.[9]

E. Genentech 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 Actemra 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 for Actemra are prohibited. If the Agency notifies Genentech that any instructional and educational materials are inconsistent with the authorized labeling, Genentech must cease distribution of such instructional and educational materials. Furthermore, as part of its notification, the Agency may also require Genentech to issue corrective communication(s).

F. Genentech will report to FDA serious adverse events and all medication errors associated with the use of Actemra for its authorized use that are reported to Genentech 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: "Actemra 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.

[9] 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. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), (7), or (8), review and concurrence 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. Genentech will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with drug product distributed under this emergency use authorization for Actemra that includes the following:

- Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or

- 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 product to meet the established specifications.

If a significant quality problem affects unreleased product and may also impact product(s) previously released and distributed, then information should be submitted for all potentially impacted lots.

Genentech will include in its notification to the Agency whether the batch, or batches, in question will be recalled.

If not included in its initial notification, Genentech must submit information confirming that Genentech has identified the root cause of the significant quality problems, taken corrective action, and provide a justification confirming that the corrective action is appropriate and effective. Genentech must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

I. Genentech will manufacture Actemra to meet all quality standards and per the manufacturing process and control strategy as detailed in Genentech's EUA request. Genentech 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 notification to and concurrence by the Agency as described under condition D.

J. Through a process of inventory control, Genentech and authorized distributor(s) will maintain records regarding distribution of Actemra (i.e., lot numbers, quantity,receiving site, receipt date).

K. Genentech and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Facilities to Whom Actemra Is Distributed and Healthcare Providers Administering Actemra

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 Fact Sheets are made available to healthcare providers and to patients, parents, and caregivers, respectively, through appropriate means, prior to administration of Actemra.

M. Healthcare facilities and healthcare providers receiving Actemra will track serious adverse events that are considered to be potentially attributable to Actemra 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, "Actemra use for COVID-19 under Emergency Use Authorization" at the beginning of the question "Describe Event" for further analysis. A copy of the completed FDA Form 3500 should also be provided to Genentech per the instructions in the authorized labeling.

N. Healthcare facilities and healthcare providers will ensure that appropriate storage and cold chain is maintained until the product is administered consistent with the terms of this letter and the authorized labeling.

O. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensing and administration of Actemra for the use authorized in this letter (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).

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

Conditions Related to Printed Matter, Advertising, and Promotion

Q. All descriptive printed matter, advertising, and promotional materials relating to the use of Actemra under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the Act, as applicable, and FDA implementing regulations. References to "approved labeling", "permitted labeling" or similar terms in these requirements shall be understood to refer to the authorized labeling for the use of Actemra under this authorization. In addition, such materials shall:

- Be tailored to the intendedaudience.
- Not take the form of reminder advertisements, as that term is described in 21 CFR 202.1(e)(2)(i), 21 CFR 200.200 and 21 CFR 201.100(f).
- Present the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts ofthe presentation for advertising and promotional materials inaudio-visual format.

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- Be accompanied by the authorized labeling, if the promotional materials are not subject to Section 502(n) of the Act.
- Be submitted to FDA accompanied by Form FDA-2253 at the time of initial dissemination or first use.

If the Agency notifies Genentech that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions Q-S of this EUA, Genentech must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency's notification. Furthermore, as part of its notification, the Agency may also require Genentech to issue corrective communication(s).

R. No descriptive printed matter, advertising, or promotional materials relating to the use of Actemra under this authorization may represent or suggest that Actemra is safe or effective when used for the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.

S. All descriptive printed matter, advertising, and promotional material, relating to the use of Actemra under this authorization clearly and conspicuously shall state that:

- Actemra has not been approved, but has been authorized for emergency use by FDA under an EUA, to treat COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO; and

- The emergency use of Actemra is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization 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 biological products during the COVID-19 pandemic 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

Dated: July 30, 2021.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2021–16705 Filed 8–4–21; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Center for Advancing Translational Sciences; Notice of Closed Meeting

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

The meeting 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 cooperative agreement applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the cooperative agreement applications, the disclosure of which would