FDA reissued the Letter of Authorization on the following dates: February 3, 2021,[4] February 25, 2021,[5] June 3, 2021,[6] July 30, 2021,[7] September 9, 2021,[8] and November 17, 2021.[9]

On January 24, 2022, again having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the November 17, 2021 letter in its entirety, to further limit the use of REGEN-COV for treatment of COVID-19 or as post-exposure prophylaxis of COVID-19 to exclude geographic regions where, based on available information including variant susceptibility to this drug and regional variant frequency, infection or exposure is likely due to a variant that is non-susceptible to REGEN-COV. Corresponding revisions have also been made to the authorized Fact Sheets.

Based on the review of the analysis of phase 3 data from COV-2067[10] (NCT04425629), a phase 1/2/3 randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of a single intravenous infusion of 600 mg casirivimab and 600 mg imdevimab in outpatients (non-hospitalized) with SARS-CoV-2 infection, it is reasonable to believe that REGEN-COV may be effective 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

[4] In the February 3, 2021 revision, FDA revised the condition on requesting changes to this authorization, including changes to the authorized Fact Sheets. New conditions were also incorporated relating to the development of instructional or educational materials, as well as certain mandatory reporting requirements for healthcare facilities and providers. In addition to certain editorial and/or clarifying revisions, the Fact Sheet for Healthcare Providers was revised to include information on the new mandatory reporting requirements on therapeutics information and utilization data for healthcare facilities and providers. Updated safety information and details on possible side effects were also incorporated into the authorized Fact Sheets.

[5] In the February 25, 2021 revision, FDA revised the condition on instructional and educational materials. New conditions were also incorporated on the establishment of a process for monitoring genomic databases for the emergence of global viral variants of SARS-CoV-2 and the assessment, if requested by FDA, of the activity of the authorized REGEN-COV against any global SARS-CoV-2 variant(s) of interest.

[6] In the June 3, 2021 revision, FDA revised the authorized use statement for REGEN-COV. Additionally, FDA authorized a change in dosing of REGEN-COV from 2400 mg (1200 mg casirivimab and 1200 mg imdevimab) to 1200 mg (600 mg casirivimab and 600 mg imdevimab), and the addition of a new presentation consisting of a single vial containing casirivimab and imdevimab co-formulated in a 1:1 ratio for either intravenous infusion or subcutaneous injection. New conditions were incorporated on the provision of samples of the authorized REGEN-COV to the U.S. Department of Health and Human Services, upon request, and the submission of certain genomic sequencing and virology information to the FDA by a specified date. Revisions to existing conditions on advertising and promotion and manufacturing practices and other editorial changes were also incorporated.

[7] In the July 30, 2021 revision, FDA authorized REGEN-COV for emergency use as post-exposure prophylaxis for COVID-19 in certain adults and pediatric individuals. Clarifying revisions to the conditions on good manufacturing practices as well as advertising and promotion were also incorporated.

[8] In the September 9, 2021 revision, FDA authorized a co-packaged presentation of REGEN-COV which consists of individual vials of both casirivimab and imdevimab inside a single carton. FDA also authorized a document entitled *Casirivimab and Imdevimab Co-Packaged Product Quick Reference Guide* that must accompany in hardcopy format the authorized co-packaged formulation of REGEN-COV that is labeled "For pandemic use". Revisions to the Fact Sheet for Healthcare Providers associated with the co-packaged presentation of REGEN-COV and clarifying revisions on the preparation of more than one dose from a single-dose vial were also incorporated.

[9] In the November 17, 2021 revision, FDA revised the product description in this Letter of Authorization with updated storage and handling information for the authorized dose pack bags of REGEN-COV, co-packaged REGEN-COV, and subcutaneous injection presentation of REGEN-COV. Corresponding revisions on storage and handling of the subcutaneous injection presentation of REGEN-COV and minor revisions to section 15 ("Virology") were also incorporated in the Fact Sheet for Healthcare Providers.

[10] Referred to as trial R10933-10987-COV-2067 in previous iterations of this Letter of Authorization.

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 REGEN-COV outweigh the known and potential risks of such product.

Additionally, based on the review of the topline analysis of phase 3 data from COV-2069 (NCT04452318), a phase 3 randomized, double-blind, placebo-controlled trial in household contacts with close exposure to a household member known to be infected with SARS-CoV-2 (index case), but who were themselves asymptomatic; and the analysis of phase 1 data from COV-2093 (NCT 04519437), an ongoing, phase 1, randomized, double-blind, placebo-controlled clinical trial assessing the safety and pharmacokinetics of repeat subcutaneous doses of REGEN-COV in subjects who are SARS-CoV-2 negative at baseline, it is reasonable to believe that REGEN-COV may be effective for use as post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, as described in the Scope of Authorization (Section II), and that, when used under such conditions, the known and potential benefits of REGEN-COV 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 REGEN-COV for treatment and as post-exposure prophylaxis of COVID-19, as described in the Scope of Authorization (Section II) and subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of REGEN-COV for treatment and as post-exposure prophylaxis 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 the following:

    - REGEN-COV may be effective 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, as further described in the Scope of Authorization (Section II)

    - REGEN-COV may be effective for use as post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, as further described in the Scope of Authorization (Section II)

And that, when used under the conditions described in the Scope of Authorization (Section II), the known and potential benefits of REGEN-COV outweigh the known and potential risks of such products; and

3. There is no adequate, approved, and available alternative to the emergency use of REGEN-COV for treatment and as post-exposure prophylaxis of COVID-19, as described in the Scope of Authorization (Section II).[11]

II. Scope of Authorization

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

- Distribution of the authorized REGEN-COV will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. Regeneron will supply REGEN-COV to authorized distributor(s)[12], who will distribute to healthcare facilities or healthcare providers as directed by the U.S. Government, in collaboration with state and local government authorities as needed;

Treatment of COVID-19

- REGEN-COV 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 progressing to severe COVID-19, including hospitalization or death;

  The monoclonal antibodies that comprise REGEN-COV, casirivimab and imdevimab, may only be administered together;

- REGEN-COV is **not** authorized for use in the following patient populations[13]:
  - 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.

- REGEN-COV is **not** authorized for treatment of mild to moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible

[11] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.
[12] "Authorized Distributor(s)" are identified by Regeneron as an entity or entities allowed to distribute authorized REGEN-COV.
[13] Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

SARS-CoV-2 variant, based on available information including variant susceptibility to this drug and regional variant frequency.[14]

- REGEN-COV 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.

- REGEN-COV is authorized for intravenous infusion. Subcutaneous injection is authorized as an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.

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

Post-Exposure Prophylaxis

- REGEN-COV may only be used in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) for post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:

    - not fully vaccinated[15] **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications[16]) **and**
        - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC)[17] **or**
        - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other

[14] FDA will monitor conditions to determine whether use in a geographic region is consistent with this scope of authorization, referring to available information, including information on variant susceptibility (see, e.g., section 15 of authorized Fact Sheet for Healthcare Providers), and the CDC regional variant frequency data available at: https://covid.cdc.gov/covid-data-tracker/#variant-proportions. FDA's determination and any updates will be available at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs.

[15] Individuals are considered to be fully vaccinated 2 weeks after their second vaccine dose in a 2-dose series (such as the Pfizer or Moderna vaccines), or 2 weeks after a single-dose vaccine (such as the Johnson & Johnson/ Janssen vaccine). See this website for more details: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html#vaccinated.

[16] See this website for more details: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

[17] Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (sneezing or coughing, for example). See this website for additional details: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html

individuals in the same institutional setting (for example, nursing homes, prisons).

- The monoclonal antibodies that comprise REGEN-COV, casirivimab and imdevimab, may only be administered together;

- REGEN-COV is **not** authorized for post-exposure prophylaxis of COVID-19 in geographic regions where exposure is likely to have been to a non-susceptible SARS-CoV-2 variant, based on available information including variant susceptibility to these drugs and regional variant frequency.[18]

- REGEN-COV 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.

- REGEN-COV is authorized for either intravenous infusion or subcutaneous injection when administered for post-exposure prophylaxis under this authorization.

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

- Post-exposure prophylaxis with REGEN-COV (casirivimab with imdevimab) is **not** intended to be a substitute for vaccination against COVID-19.

- REGEN-COV is **not** authorized for pre-exposure prophylaxis for prevention of COVID-19.

Product Description

Casirivimab and imdevimab are recombinant neutralizing human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2. REGEN-COV is available in three distinct presentations: (1) REGEN-COV co-packaged in an individual carton, (2) REGEN-COV in dose pack bags, and (3) co-formulated solution of REGEN-COV.[19]

[18] Supra at Note 14.

[19] Individual vials of casirivimab and imdevimab distributed in interstate commerce prior to the reissuance of this letter on February 3, 2021 remain authorized for emergency use. FDA is not requiring that such product be repackaged given the public health need for the product. The use of the individual vials of casirivimab and imdevimab must be consistent with the terms and conditions of this authorization. Individual vial labels for casirivimab and imdevimab and carton labeling may be clearly marked with either "Caution: New Drug - Limited by Federal (or United States) law to investigational use" or with "For use under Emergency Use Authorization (EUA)". Some vial labels and carton labeling of casirivimab and imdevimab may be instead labeled with the Investigational New Drug (IND) clinical trial code name as "REGN10933" and "REGN10987", respectively.

(1) *Co-packaged REGEN-COV:* Co-packaged REGEN-COV is comprised of one vial each of both casirivimab and imdevimab inside a single carton. Individual vial and carton container labeling for casirivimab and imdevimab covered in the authorized co-packaged presentation will be clearly marked with either "For pandemic use" or "For Use under Emergency Use Authorization."

Casirivimab is available as 300 mg/2.5 mL (120 mg/mL) or 1332 mg/11.1 mL (120 mg/mL) sterile, preservative-free aqueous solution to be diluted prior to infusion. Imdevimab is available as 300 mg/2.5 mL (120 mg/mL) or 1332 mg/11.1 mL (120 mg/mL) sterile, preservative-free aqueous solution to be diluted prior to infusion. Co-packaged REGEN-COV supplied in the 1332 mg/11.1 mL strength presentation will include a sufficient number of vials of casirivimab and imdevimab to prepare more than one dose.

The authorized storage and handling information for the co-packaged REGEN-COV is included in the authorized Fact Sheet for Healthcare Providers.

(2) *Dose pack bags:* Dose pack bags of REGEN-COV will include a sufficient number of vials of casirivimab and imdevimab to prepare more than one dose. Individual vials and carton container labeling for casirivimab and imdevimab included in dose pack bags are clearly marked "For Use under Emergency Use Authorization." Casirivimab and imdevimab are recombinant neutralizing human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2.

Casirivimab is available as 300 mg/2.5 mL (120 mg/mL) or 1332 mg/11.1 mL (120 mg/mL) sterile, preservative-free aqueous solution to be diluted prior to infusion. Imdevimab is available as 300 mg/2.5 mL (120 mg/mL) or 1332 mg/11.1 mL (120 mg/mL) sterile, preservative-free aqueous solution to be diluted prior to infusion.

The authorized storage and handling information for the dose pack bags of REGEN-COV is included in the authorized Fact Sheet for Healthcare Providers.

(3) *Co-formulated solution of REGEN-COV*: The co-formulated solution of REGEN-COV contains two antibodies in a 1:1 ratio in a single dose vial consisting of 600 mg casirivimab and 600 mg of imdevimab per 10 mL (60 mg/60 mg per mL). Individual vials of co-formulated REGEN-COV are clearly marked "For Use under Emergency Use Authorization."

Co-formulated casirivimab and imdevimab is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution. Co-formulated REGEN-COV may be administered via intravenous infusion or subcutaneous injection.

The authorized storage and handling information for the co-formulated solution of REGEN-COV is included in the authorized Fact Sheet for Healthcare Providers.

Any presentation of REGEN-COV described above may be prepared for intravenous infusion or subcutaneous injection.[20]

[20] Certain carton labeling for the co-packaged presentation of REGEN-COV is labeled as "casirivimab and

REGEN-COV is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and patients/caregivers, respectively, through Regeneron's website at www.REGENCOV.com:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of REGEN-COV (casirivimab and imdevimab)

- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of REGEN-COV (casirivimab and imdevimab) for Coronavirus Disease 2019 (COVID-19)

The co-packaged presentation of REGEN-COV that is labeled "For pandemic use" is also authorized for emergency use with the document entitled *Casirivimab and Imdevimab Co-Packaged Product Quick Reference Guide*, which must accompany this authorized co-packaged presentation of REGEN-COV in hardcopy format.

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 REGEN-COV, when used for treatment and as post-exposure prophylaxis of COVID-19 as described in 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 REGEN-COV may be effective for treatment and as post-exposure prophylaxis 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 REGEN-COV (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), REGEN-COV is authorized for treatment and as post-exposure prophylaxis of COVID-19 as described in this 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:

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imdevimab 120 mg/mL concentrate for solution for infusion. The vials in the carton for the co-packaged presentation of REGEN-COV may be used to prepare and administer REGEN-COV for either intravenous infusion or subcutaneous injection despite this labeling.

Regeneron and Authorized Distributors

A. Regeneron and authorized distributor(s) will ensure that the authorized REGEN-COV is distributed as directed by the U.S. government, and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers consistent with the terms of this letter.

B. Regeneron 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. Regeneron 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 REGEN-COV. Regeneron will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (i.e., Fact Sheets).

D. Regeneron may request changes to this authorization, including to the authorized Fact Sheets for REGEN-COV. 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.[21]

E. Regeneron 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 REGEN-COV 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 REGEN-COV are prohibited. Should the Agency become aware of any instructional or educational materials that are inconsistent with the authorized labeling for REGEN-COV, the Agency will require Regeneron to cease distribution of such instructional and educational materials.

[21] 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.

F. Regeneron will report to FDA serious adverse events and all medication errors associated with the use of the authorized REGEN-COV that are reported to Regeneron 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 must state: "REGEN-COV 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.

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. Regeneron will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with distributed drug product of REGEN-COV 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 must be submitted for all potentially impacted lots.

Regeneron 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, Regeneron must recall them.

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

I. Regeneron will manufacture REGEN-COV to meet all quality standards and per the manufacturing process and control strategy as detailed in Regeneron's EUA request.

Regeneron 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. Regeneron will list the single dose pack bag, the co-packaged product, and the co-formulated product containing casirivimab and imdevimab with unique NDC product codes from each other and the NDC product codes of the single ingredient listings under the marketing category of Unapproved Drug-Other. As applicable, different vial sizes should be identified by a different package NDC within the product NDC. 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, Regeneron and authorized distributor(s) will maintain records regarding distribution of the authorized casirivimab and imdevimab (i.e., lot numbers, quantity, receiving site, receipt date).

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

M. Regeneron will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2. A summary of Regeneron'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. Regeneron 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 Regeneron to assess the activity of the authorized REGEN-COV 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). Regeneron will perform the required assessment in a manner and timeframe agreed upon by Regeneron and the Agency. Regeneron 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. Regeneron 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. Regeneron shall provide samples as requested of the authorized REGEN-COV 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 REGEN-COV 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. Regeneron will submit to FDA all sequencing data assessing REGEN-COV, including sequencing of any participant samples from the full analysis population from COV-2067 that have not yet been completed no later than July 30, 2021. Regeneron will provide the Agency with a frequency table reporting all substitutions detected for all participants at all available time points at a frequency ≥5%.

Q. Regeneron will submit to FDA all SARS-CoV-2 nasopharyngeal viral shedding and blood viral load data, including quantitation of viral load for any participant samples from the full analysis population for which REGEN-COV is currently authorized from COV-2067 that have not yet been completed, no later than July 30, 2021.

Healthcare Facilities to Whom the Authorized REGEN-COV Is Distributed and Healthcare Providers Administering the Authorized Casirivimab and Imdevimab

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 REGEN-COV.

S. Healthcare facilities and healthcare providers receiving REGEN-COV will track serious adverse events and medication errors that are considered to be potentially attributable to REGEN-COV 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 must state, "REGEN-COV 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 REGEN-COV (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 Regeneron and/or FDA. Such records will be made available to Regeneron, HHS, and FDA for inspection upon request.

W. Healthcare facilities and providers will report therapeutics information and utilization data as directed by the U.S. Department of Health and Human Services.

Conditions Related to Printed Matter, Advertising and Promotion

X. All descriptive printed matter, advertising, and promotional materials relating to the use of the REGEN-COV 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, as applicable. 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 REGEN-COV under this authorization. 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 the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts of the presentation for advertising and promotional materials in audio-visual format.
- 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 Regeneron that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions X-Z of this EUA, Regeneron 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 Regeneron to issue corrective communication(s).

Y. No descriptive printed matter, advertising, or promotional materials relating to the use of REGEN-COV under this authorization may represent or suggest that REGEN-COV is safe or effective when used for the treatment of COVID-19 or when used as post-exposure prophylaxis as described in the Scope of Authorization (Section II).

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

- REGEN-COV has not been approved, but has been authorized for emergency use by FDA under an EUA, for treatment and as post-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg) with high risk for progression to severe COVID-19, including hospitalization or death, and

- The emergency use of REGEN-COV 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,

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Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration