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Part II

Department of Health and Human Services

Food and Drug Administration

**Amended Authorizations of Emergency
Use of Zanamivir, Oseltamivir Phosphate,
and Peramivir; Authorization of
Emergency Use of Certain In Vitro
Diagnostic Devices; Availability; Notices**

DEPARTMENT OF HEALTH AND HUMAN SERVICES**Food and Drug Administration**

[Docket No. FDA-2009-N-0276]

Amended Authorizations of Emergency Use of Certain Antiviral Drugs Zanamivir and Oseltamivir Phosphate; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing amendments to the two Emergency Use Authorizations (EUAs) (the Authorizations) for certain products from the neuraminidase class of antivirals, zanamivir and oseltamivir phosphate, issued on April 27, 2009, under the Federal Food, Drug, and Cosmetic Act (the act), as requested by the Centers for Disease Control and Prevention (CDC). On July 14, 2009, in response to a request from CDC, FDA amended and reissued in its entirety the Authorization for certain oseltamivir phosphate products. On October 30, 2009, in response to a request from CDC, among other reasons, FDA amended and reissued in their entirety the Authorization letters for certain zanamivir and oseltamivir phosphate products. Finally, on November 4, 2009, FDA amended and reissued in its entirety the Authorization letter for certain zanamivir inhalation powder. The Authorization letter for certain oseltamivir phosphate products, as amended on October 30, 2009, and the Authorization letter for certain zanamivir inhalation powder, as amended on November 4, 2009, including explanations for their reissuance, are reprinted in this document.

DATES: The amended Authorizations are effective as of October 30, 2009.

ADDRESSES: Submit written requests for single copies of the EUAs to the Office of Counterterrorism and Emerging Threats (HF-29), Food and Drug Administration, 5600 Fishers Lane, rm. 14C-26, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your request or include a fax number to which the Authorization(s) may be sent. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the Authorizations.

FOR FURTHER INFORMATION CONTACT: RADM Boris Lushniak, Office of Counterterrorism and Emerging Threats (HF-29), Food and Drug

Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4067.

SUPPLEMENTARY INFORMATION:**I. Amendment to the April 27, 2009, Authorizations for Certain Products From the Neuraminidase Class of Antivirals, Zanamivir and Oseltamivir Phosphate**

On April 26, 2009, under section 564(b)(1)(C) of the act (21 U.S.C. 360bbb-3(b)(1)(C)), the Acting Secretary of the Department of Health and Human Services (the Acting Secretary) determined that a public health emergency exists involving Swine Influenza A (now known as 2009 H1N1 Influenza A or 2009 H1N1 flu) that affects, or has the significant potential to affect, national security. The determination of emergency has been renewed. On April 26, 2009, under section 564(b) of the act, and on the basis of such determination, the Acting Secretary declared an emergency justifying the authorization of the emergency use of certain products from the neuraminidase class of antivirals, zanamivir and oseltamivir phosphate, accompanied by emergency use information subject to the terms of any authorization issued under 21 U.S.C. 360bbb-3(a). On April 26, 2009, CDC requested and, on April 27, 2009, FDA issued EUAs for zanamivir inhalation powder and certain oseltamivir phosphate capsules and oral suspension for the treatment and prophylaxis of influenza, accompanied by emergency use instructions, which are authorized under the EUAs. On April 27, 2009, FDA also amended the EUAs for zanamivir and oseltamivir phosphate, including the emergency use instructions authorized under the EUAs. On August 4, 2009, notice of the determination and declaration was published in the **Federal Register** (74 FR 38628, August 4, 2009), as was the notice of the April 27, 2009, Authorizations (74 FR 38648, August 4, 2009).

On July 7, 2009, CDC submitted a request to amend the Authorization for certain oseltamivir phosphate products to address, among other things, issues relating to certain oseltamivir phosphate oral suspension products that had passed testing under the Federal Government's Shelf Life Extension Program for use beyond their expiration dates. In response to CDC's request, on July 14, 2009, FDA amended the Authorization letter and reissued the Authorization letter in its entirety. Because the subsequent October 30, 2009, amendment to the Authorization for certain oseltamivir phosphate

products incorporated the July 2009 amendment in its entirety, the July 2009 amendment to the Authorization letter for certain oseltamivir phosphate products is not reprinted in this document.

On October 29, 2009, CDC submitted another request to amend both of the Authorizations for certain zanamivir and oseltamivir phosphate products to address, among other things, issues relating to certain zanamivir inhalation powder and oseltamivir phosphate capsules deployed from the Strategic National Stockpile (SNS) that were beyond or would be beyond their expiration date before the declaration of emergency underlying the EUA terminated. FDA also became aware of other zanamivir inhalation powder and oseltamivir phosphate capsules in addition to those held in or deployed from the SNS that were beyond or would be beyond their expiration date before the declaration of emergency underlying the EUA terminated. FDA amended both of the Authorization letters to address both of these categories products. Among the other reasons that FDA amended the Authorization for certain oseltamivir phosphate products was to update the information for health care providers to include dosing recommendations based on weight for children younger than 1 year of age. Therefore, in response to CDC's October 2009 request, among other reasons, FDA amended and reissued both of the Authorization letters in their entirety on October 30, 2009. Finally, on November 4, 2009, to include a condition of Authorization inadvertently omitted, FDA again amended the Authorization letter for certain zanamivir inhalation powder.

II. Electronic Access

An electronic version of this document and the full text of the Authorizations are available on the Internet at <http://www.regulations.gov>.

III. The Authorizations

Having concluded that the criteria for issuance of the Authorizations under section 564(c) of the act were met, on April 27, 2009, FDA authorized the emergency use of certain zanamivir inhalation powder and certain oseltamivir phosphate capsules and oral suspension for the treatment and prophylaxis of influenza, accompanied by emergency use information, subject to the terms and conditions of the authorizations.

The Authorization (as amended on October 30, 2009) for certain oseltamivir phosphate capsules and oral suspension follows and provides an explanation of

the reasons for its issuance, as required by section 564(h)(1) of the act:

October 30, 2009

Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
Atlanta, GA 30333

Dear Dr. Frieden:

On April 27, 2009, a letter was issued authorizing the emergency use of certain oseltamivir phosphate capsules and oral suspension for treatment and prophylaxis of influenza subject to the terms of that letter. On the same day, an amendment to the letter was also issued.¹ On July 14, 2009, an amendment to the letter was issued addressing certain oseltamivir phosphate products identified by FDA that have passed testing under the federal government's Shelf Life Extension Program (SLEP). I am issuing this letter in response to your October 29, 2009 request to address, among other things, issues that have arisen relating to certain oseltamivir phosphate capsules deployed from the Strategic National Stockpile (SNS) that are beyond or will be beyond their expiration date before the declaration of emergency underlying this EUA has terminated. FDA has also become aware of certain oseltamivir phosphate capsules in addition to those held in or deployed from the Strategic National Stockpile that are beyond or will be beyond their expiration date before the declaration of emergency underlying the EUA has terminated. FDA is issuing this amendment to address both of these categories of oseltamivir phosphate capsules, as further described below. The letter of authorization, as amended, appears below in its entirety:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of certain oseltamivir phosphate capsules and oral suspension for treatment and prophylaxis of influenza, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On April 26, 2009, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (DHHS) determined that a public health emergency exists involving Swine Influenza A (now called 2009-H1N1 flu) that affects or has significant potential to affect national security. Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of DHHS then declared an emergency justifying the authorization of the emergency use of certain oseltamivir phosphate products subject to the terms of any authorization issued under section 564(a) of the Act (21 U.S.C. § 360bbb-3(a)). The Secretary's determination of emergency has been renewed. The Secretary's April 26, 2009 declaration of emergency justifying an EUA remains in effect.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(b)) are met, I am authorizing the emergency use of certain oseltamivir phosphate products² for the treatment and prophylaxis of influenza, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of certain oseltamivir phosphate products for the treatment and prophylaxis of influenza meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) 2009-H1N1 flu can cause influenza, a serious or life-threatening disease or condition;
- (2) Based on the totality of scientific evidence available to FDA, it is reasonable to believe that certain oseltamivir phosphate products may be effective for the treatment and prophylaxis of influenza, and that the known and potential benefits of certain oseltamivir phosphate products, when used for the treatment and prophylaxis of influenza, outweigh the known and potential risks of such products; and
- (3) There is no adequate, approved, and available alternative to the emergency use of certain oseltamivir phosphate products for the treatment and prophylaxis of influenza.³

Therefore, I have concluded that the emergency use of certain oseltamivir phosphate products for the treatment and prophylaxis of influenza meets the above statutory criteria for issuance of an authorization.

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of authorized oseltamivir phosphate products for the treatment and prophylaxis of influenza for individuals exposed to 2009-H1N1 flu. The emergency use of authorized oseltamivir phosphate products under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below.

The authorized oseltamivir phosphate products are as follows:

- Tamiflu (oseltamivir phosphate) (30 mg, 45 mg, and 75 mg) capsules
- Tamiflu (oseltamivir phosphate) oral suspension

Oseltamivir phosphate products are approved and indicated for the treatment of uncomplicated acute illness due to influenza infections in patients 1 year and older who have been symptomatic for no more than 2 days. Oseltamivir phosphate products are also approved and indicated for the prophylaxis of influenza in patients 1 year and older.⁴

1. The above oseltamivir phosphate products are authorized for use in patients less than 1 year old. Such products are also authorized for use at later time points (i.e., patients who are symptomatic for more than 2 days) and/or in patients sick enough to require hospitalization (i.e., patients who do not have "uncomplicated acute illness" per se).
2. The above oseltamivir phosphate products labeled consistent with the manufacturer's label are authorized to be distributed under this EUA. Such products are authorized to be distributed or dispensed without the requisite prescription label information under section 503(b)(2) of the Act (e.g., name and address of dispenser, serial number, date of prescription or of its filling, name of prescriber, name of patient, if stated on prescription, directions for use and cautionary statements, if contained in the prescription), except for product described in paragraph 3c. below that is held by entities that are not public health authorities.
- 3a. The above oseltamivir phosphate products may include products that are deployed from the SNS and that have passed testing under the federal government's Shelf Life Extension Program (SLEP) for use beyond their expiration dates.
- 3b. Certain oseltamivir phosphate products that are: (i) identified by FDA, (ii) deployed from the SNS, and (iii) have passed SLEP testing are authorized to be distributed or dispensed without information on the label about the use of the products beyond their expiration dates. The appropriate public health authorities are authorized to label these products with information about the use of the products beyond their expiration dates should the appropriate public health authorities choose to do so.
- 3c. Certain oseltamivir phosphate capsules that are (i) identified by FDA and (ii) are beyond or will be beyond their expiration dates before the declaration of emergency underlying this EUA has terminated are authorized to be distributed or dispensed subject to the terms and conditions of this authorization.
4. The above oseltamivir phosphate products are authorized to be accompanied by the following written information pertaining to the emergency use, which are authorized to be made available to health care providers⁵ and recipients:
 - Fact Sheet for Health Care Provider
 - Fact Sheet for Patients and Parents/Caretakers

CDC and the appropriate public health authorities are also authorized to make available additional information relating to the emergency use of authorized oseltamivir phosphate products that is consistent with, and does not exceed, the terms of this letter of authorization. (See section IV).

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 authorized oseltamivir phosphate products, when used for the treatment and prophylaxis of influenza, outweigh the known and potential risks of such products.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized oseltamivir phosphate products may be effective for the treatment and prophylaxis of influenza pursuant to section 564(c)(2)(A) of the Act. FDA has reviewed the scientific information available, including the information supporting the conclusions described in Section I above, and concludes that the authorized oseltamivir phosphate products, when used for the treatment and prophylaxis of influenza in the specified population, meet the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.⁶

Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHHS's determination under section 564(b)(1)(C) described above and the Secretary of DHHS's corresponding declaration under section 564(b)(1), the oseltamivir phosphate products described above are authorized for the treatment and prophylaxis of influenza for individuals exposed to 2009-H1N1 flu.

This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Current Good Manufacturing Practice

In the letter dated April 27, 2009, current good manufacturing practice (CGMP) requirements were waived with respect to the holding of authorized oseltamivir phosphate products by CDC and other public health authorities for a period of ninety days (the "First Waiver"). As of the date of the July 14, 2009 letter, I terminated the First Waiver and replaced it with the following waiver, which remains in effect:

Although authorized oseltamivir phosphate products should be held in accordance with CGMP holding requirements, including appropriate product storage conditions⁷, I am waiving CGMP requirements with respect to the holding of authorized oseltamivir phosphate products by CDC and other public health authorities for a maximum of 90 days (consecutive or non-consecutive) from the date of shipment to the public health authority. However, this waiver is also limited in that the products may be stored with temperature excursions in excess of 40°C for a total cumulative period of 14 days (consecutive or non-consecutive) within that 90 days. Other temperature excursions outside labeled temperature storage conditions and not in excess of 40°C are permitted within the 90-day period.

IV. Conditions of Authorization

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

CDC

- A. CDC will verify that oseltamivir phosphate products distributed to the Receive, Stage, Storage (RSS) sites:
 - (i) are within unexpired labeled dates,
 - (ii) have passed SLEP testing, whether relabeled or not, and are within the dates supported by SLEP testing, or
 - (iii) are beyond or will be beyond their expiration dates before the termination of the Secretary's declaration of emergency and have been identified by FDA under Section II.3.c.

- B. For oseltamivir phosphate products identified in Section II.3.b. and c. of this letter, information on the lot numbers of the oseltamivir phosphate products identified by FDA will be made available by CDC to the appropriate public health authorities, healthcare providers, and recipients (patients and parents) through appropriate means.
- C. CDC will ensure that the appropriate public health authorities are informed of this EUA, including the terms and conditions herein.
- D. CDC will make available to the appropriate public health authorities through appropriate means the authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents/Caretakers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized oseltamivir phosphate products.
- E. Only CDC may request changes to the authorized Fact Sheet for Health Care Providers and authorized Fact Sheet for Patients and Parents/Caretakers. Such requests will be made by contacting FDA concerning FDA review and approval.

Public Health Authorities⁸

- F. The appropriate public health authorities will ensure that authorized oseltamivir phosphate products are distributed to recipients in accordance with applicable laws and/or in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and their officials, agents, employees, contractors, or volunteers following a declaration of an emergency.⁹ However, the appropriate public health authorities will ensure that authorized oseltamivir phosphate products are distributed, dispensed, and/or administered to patients less than 1 year old only under the supervision of a licensed healthcare provider.
- G. The appropriate public health authorities will make available through appropriate means authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents/Caretakers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized oseltamivir phosphate products.
- H. The appropriate public health authorities are authorized to label the oseltamivir phosphate products identified in Section II.3.b. with information about the use of the products beyond their expiration dates, should the appropriate public health authorities choose to do so.

Entities That Are Not Public Health Authorities

- I. Entities acting under Section II.3.c. that are neither (a) public health authorities nor (b) acting in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures will ensure that authorized oseltamivir phosphate capsules are prescribed and dispensed to recipients in accordance with applicable laws that are consistent with this letter of authorization and with applicable federal public health guidelines that are consistent with this letter of authorization.
- J. Entities acting under Section II.3.c. that are neither (a) public health authorities nor (b) acting in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and that dispense authorized oseltamivir phosphate products, will make available through appropriate means the authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized oseltamivir phosphate capsules.
- K. Entities acting under Section II.3.c. that are neither (a) public health authorities nor (b) acting in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and that dispense authorized oseltamivir phosphate products, will verify that the oseltamivir phosphate products that are beyond or will be beyond their expiration dates before the termination of the Secretary's declaration of emergency have been identified by FDA under Section II.3.c.

CDC and Public Health Authorities

- L. CDC and the appropriate public health authorities are also authorized to make available additional information relating to the emergency use of authorized oseltamivir phosphate products that is consistent with, and does not exceed, the terms of this letter of authorization.

The emergency use of authorized oseltamivir phosphate products as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs

¹ Specifically, the letter was amended in the following two respects: (1) the reference on page 3 to "Fact Sheet for Patients and Recipients" was revised to read "Fact Sheet for Patients and Parents"; and (2) the correct authorized versions of the Tamiflu Fact Sheet for Health Care Providers and Tamiflu Fact Sheet for Patients and Parents were attached to the letter.

² FDA is authorizing the emergency use of Tamiflu (oseltamivir phosphate) (30 mg, 45 mg, and 75 mg) capsules and oral suspension for treatment and prophylaxis of influenza as described in the scope section of this letter (Section II). For ease of reference, this letter of authorization will use the terms "certain oseltamivir phosphate product(s)" and "authorized oseltamivir phosphate product(s)."

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

⁴ The approved labeling also states the following: "The following points should be considered before initiating treatment or prophylaxis with [oseltamivir phosphate products]: [Oseltamivir phosphate products are] not a substitute for early vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices. Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use [oseltamivir phosphate products.]"

⁵ It is possible that public health officials or other volunteers might distribute authorized oseltamivir phosphate products to recipients (except as limited in IV.F below), if permitted, in accordance with applicable state and local law and/or in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and their officials, agents, employees, contractors, or volunteers following a declaration of an emergency. For ease of reference, this letter will use the term "health care provider(s)" to refer collectively to these individuals.

⁶ Please note that with respect to authorized oseltamivir phosphate products for use in patients less than 1 year old, the conclusions above are based on limited data available for review under the limited timeframe given the circumstances of the emergency. The conclusions above may evolve as the emergency circumstances evolve and as more information becomes available.

⁷ See Tamiflu Capsule and Oral Suspension product labeling or http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021087s047,%20021246s033bl.pdf for oseltamivir phosphate product storage conditions.

⁸ Conditions F, G, and H apply to entities that are not public health authorities, but are acting under the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures.

⁹ For more information about the terms "Authority Having Jurisdiction" and "covered countermeasures," see Public Readiness and Emergency Preparedness (PREP) Act, sections 319F-3 and 319F-4 of the Public Health Service Act (codified at 42 U.S.C. §§ 247d-6d, 247d-6e), and the PREP Act declaration regarding pandemic influenza antivirals. See <http://www.hhs.gov/disasters/discussion/planners/prepac/>.

The Authorization (as amended on November 4, 2009) for certain zanamivir inhalation powder follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

November 4, 2009

Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
Atlanta, GA 30333

Dear Dr. Frieden:

On April 27, 2009, a letter was issued authorizing the emergency use of certain zanamivir inhalation powder for treatment and prophylaxis of influenza subject to the terms of that letter. On the same day, an amendment to the letter was also issued.¹ On October 30, 2009, the Food and Drug Administration (FDA) issued an amendment to the April letter in response to your October 29, 2009 request to address, among other things, issues that have arisen relating to certain zanamivir products deployed from the Strategic National Stockpile (SNS) that are beyond or will be beyond their expiration date before the declaration of emergency underlying this Emergency Use Authorization (EUA) has terminated. FDA had also become aware of certain zanamivir products in addition to those held in or deployed from the SNS that are beyond or will be beyond their expiration date before the declaration of emergency underlying the EUA has terminated. FDA issued the October 30, 2009 amendment to address both categories of zanamivir products, as further described below. I hereby amend the October 30 letter to include condition J below and to make other minor corrections. The letter of authorization, as amended, is being reissued in its entirety with the amendments incorporated.

This letter is in response to your request that FDA issue an EUA for the emergency use of zanamivir inhalation powder for treatment and prophylaxis of influenza, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On April 26, 2009, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (DHHS) determined that a public health emergency exists involving Swine Influenza A (now called 2009-H1N1 flu) that affects or has significant potential to affect national security. Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of DHHS then declared an emergency justifying the authorization of the emergency use of certain zanamivir products subject to the terms of any authorization issued under section 564(a) of the Act (21 U.S.C. § 360bbb-3(a)). The Secretary's determination of emergency has been renewed. The Secretary's April 26, 2009 declaration of emergency justifying an EUA remains in effect.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(b)) are met, I am authorizing the emergency use of certain zanamivir products² for the treatment and prophylaxis of influenza, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of certain zanamivir products for the treatment and prophylaxis of influenza meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) 2009-H1N1 flu can cause influenza, a serious or life-threatening disease or condition;
- (2) Based on the totality of scientific evidence available to FDA, it is reasonable to believe that certain zanamivir products may be effective for the treatment and prophylaxis of influenza, and that the known and potential benefits of certain zanamivir products, when used for the treatment and prophylaxis of influenza, outweigh the known and potential risks of such products; and
- (3) There is no adequate, approved, and available alternative to the emergency use of certain zanamivir products for the treatment and prophylaxis of influenza.³

Therefore, I have concluded that the emergency use of certain zanamivir products for the treatment and prophylaxis of influenza meets the above statutory criteria for issuance of an authorization.

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of authorized zanamivir products for the treatment and prophylaxis of influenza for individuals exposed to 2009-H1N1 flu. The emergency use of authorized zanamivir products under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below.

The authorized zanamivir products are as follows:

- Relenza (zanamivir) Inhalation Powder

Zanamivir products are approved and indicated for the treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients 7 years of age and older who have been symptomatic for no more than 2 days. Zanamivir products are also approved and indicated for prophylaxis of influenza in adults and pediatric patients 5 years of age and older.⁴

1. The above zanamivir products are authorized for use at later time points (i.e., patients who are symptomatic for more than 2 days) and/or in patients sick enough to require hospitalization (i.e., patients who do not have “uncomplicated acute illness” per se).
2. The above zanamivir products labeled consistent with the manufacturer’s label are authorized to be distributed under this EUA. Such products are authorized to be distributed or dispensed without the requisite prescription label information under section 503(b)(2) of the Act (e.g., name and address of dispenser, serial number, date of prescription or of its filling, name of prescriber, name of patient, if stated on prescription, directions for use and cautionary statements, if contained in the prescription), except for product described in paragraph 3 below that is held by entities that are not public health authorities.
3. Certain zanamivir products that are (i) identified by FDA and (ii) are beyond or will be beyond their expiration dates before the declaration of emergency underlying this EUA has terminated are authorized to be distributed or dispensed subject to the terms and conditions of this authorization.
4. The above zanamivir products are authorized to be accompanied by the following written information pertaining to the emergency use, which are authorized to be made available to health care providers⁵ and recipients:

- Fact Sheet for Health Care Provider
- Fact Sheet for Patients and Parents/Caregivers

CDC and the appropriate public health authorities are also authorized to make available additional information relating to the emergency use of authorized zanamivir products that is consistent with, and does not exceed, the terms of this letter of authorization. (See section IV).

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 authorized zanamivir products, when used for the treatment and prophylaxis of influenza, outweigh the known and potential risks of such products.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized zanamivir products may be effective for the treatment and prophylaxis of influenza pursuant to section 564(c)(2)(A) of the Act. FDA has reviewed the scientific information available, including the information supporting the conclusions described in Section I above, and concludes that the authorized zanamivir products, when used for the treatment and prophylaxis of influenza in the specified population, meet the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHHS’s determination under section 564(b)(1)(C) described above and the Secretary of DHHS’s corresponding declaration under section 564(b)(1), the zanamivir products described above are authorized for the treatment and prophylaxis of influenza for individuals exposed to 2009-H1N1 flu.

This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Current Good Manufacturing Practice

In the letter dated April 27, 2009, current good manufacturing practice (CGMP) requirements were waived with respect to the holding of authorized zanamivir products by CDC and other public health authorities for a period of ninety days (the “First Waiver”). As of the date of this letter, I terminate the First Waiver and replace it with the following waiver:

Although authorized zanamivir products should be held in accordance with CGMP holding requirements, including appropriate product storage conditions,⁶ I am waiving CGMP requirements with respect to the monitoring and calculating of mean kinetic temperature by CDC and other public health authorities so long as, to the extent practicable given the circumstances of the emergency, temperature is monitored. I also am waiving CGMP requirements with respect to holding at the labeled storage conditions in that the products may be stored with temperature excursions up to 40°C for a total cumulative period of 7 days (consecutive or non-consecutive) from the date of shipment to the public health authority.

IV. Conditions of Authorization

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

CDC

- A. CDC will verify that zanamivir products distributed to the Receive, Stage, Storage (RSS) sites are within their labeled expiration dates, or are beyond or will be beyond their expiration dates before the termination of the Secretary's declaration of emergency and have been identified by FDA under Section II.3.
- B. For zanamivir products identified in Section II.3 of this letter, information on the lot numbers of the zanamivir products identified by FDA will be made available by CDC to the appropriate public health authorities, healthcare providers, and recipients (patients and parents/caregivers) through appropriate means.
- C. CDC will ensure that the appropriate public health authorities are informed of this EUA, including the terms and conditions herein.
- D. CDC will make available to the appropriate public health authorities through appropriate means the authorized Fact Sheet for Health Care Providers, authorized Fact Sheet for Patients and Parents/Caregivers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized zanamivir products.
- E. Only CDC may request changes to the authorized Fact Sheet for Health Care Providers and authorized Fact Sheet for Patients and Parents/Caregivers. Such requests will be made by contacting FDA concerning FDA review and approval.

Public Health Authorities⁷

- F. The appropriate public health authorities will ensure that authorized zanamivir products are distributed to recipients in accordance with applicable laws and/or in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and their officials, agents, employees, contractors, or volunteers following a declaration of an emergency.⁸
- G. The appropriate public health authorities will make available through appropriate means authorized Fact Sheets for Health Care Providers, authorized Fact Sheets for Patients and Parents/Caregivers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized zanamivir products.

Entities That Are Not Public Health Authorities

- H. Entities acting under Section II.3 that are neither (a) public health authorities nor (b) acting in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense covered countermeasures will ensure that authorized zanamivir products are prescribed and dispensed to recipients in accordance with applicable laws that are consistent with this letter of authorization and with applicable federal public health guidelines that are consistent with this letter of authorization.
- I. Entities acting under Section II.3 that are neither (a) public health authorities nor (b) acting in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and that dispense authorized zanamivir products, will make available through appropriate means the authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents/Caregivers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized zanamivir products.
- J. Entities acting under Section II.3 that are neither (a) public health authorities nor (b) acting in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and that dispense authorized zanamivir products, will verify that the zanamivir products that are beyond or will be beyond their expiration dates before the termination of the Secretary's declaration of emergency have been identified by FDA under Section II.3.

CDC and Public Health Authorities

- K. CDC and the appropriate public health authorities are also authorized to make available additional information relating to the emergency use of authorized zanamivir products that is consistent with, and does not exceed, the terms of this letter of authorization.

The emergency use of authorized zanamivir products as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs

¹ Specifically, the letter was amended in the following respect: the correct authorized versions of the Zanamivir Fact Sheet for Health Care Providers and Zanamivir Summary Fact Sheet for Patients and Parents were attached to the letter.

² FDA is authorizing the emergency use of Relenza (zanamivir) inhalation powder for treatment and prophylaxis of influenza as described in the scope section of this letter (Section II). For ease of reference, this letter of authorization will use the terms "certain zanamivir product(s)" and "authorized zanamivir product(s)."

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

⁴ Zanamivir products are not recommended for treatment or prophylaxis of influenza in individuals with underlying airways disease (such as asthma or chronic obstructive pulmonary disease) due to risk of serious bronchospasm. Zanamivir products have not been proven effective for treatment of influenza in individuals with underlying airways disease. Zanamivir products have not been proven effective for prophylaxis of influenza in the nursing home setting. Zanamivir products are not a substitute for early vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices. Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use zanamivir products. There is no evidence for efficacy of zanamivir in any illness caused by agents other than Influenza A and B. Patients should be advised that the use of zanamivir products for treatment of influenza has not been shown to reduce the risk of transmission of influenza to others.

⁵ It is possible that public health officials or other volunteers might distribute authorized zanamivir products to recipients, if permitted, in accordance with applicable state and local law and/or in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and their officials, agents, employees, contractors, or volunteers following a declaration of an emergency. For ease of reference, this letter will use the term "health care provider(s)" to refer collectively to these individuals.

⁶ See FDA-approved product labeling for zanamivir products storage conditions (http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021036s017lbl.pdf)

⁷ Conditions F and G apply to entities that are not public health authorities, but are acting under the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures.

⁸ For more information about the terms "Authority Having Jurisdiction" and "covered countermeasures," see Public Readiness and Emergency Preparedness (PREP) Act, sections 319F-3 and 319F-4 of the Public Health Service Act (codified at 42 U.S.C. §§ 247d-6d, 247d-6e), and the PREP Act declaration regarding pandemic influenza antivirals. See <http://www.hhs.gov/disasters/discussion/planners/prepac/>.

Dated: April 9, 2010.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2010-8603 Filed 4-16-10; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2009-N-0521]

Amended Authorization of Emergency Use of the Antiviral Product Peramivir Accompanied by Emergency Use Information; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an amendment to the Emergency Use Authorization (EUA) (the Authorization) for peramivir injection 200 milligrams (mg)/20 milliliter (mL) (10 mg/mL) single use vial manufactured for BioCryst Pharmaceuticals, Inc. (BioCryst) for intravenous (IV) administration in certain adult and pediatric patients issued on October 23, 2009, under the Federal Food, Drug, and Cosmetic Act (the act), as requested by the Centers for Disease Control and Prevention (CDC). FDA received inquiries related to the recommended dosing for patients with renal impairment. On November 19, 2009, FDA amended the Authorization letter and reissued the Authorization letter in its entirety to provide additional clarification. The Authorization letter, as amended and reissued, which includes explanations for its reissuance, is reprinted in this notice.

DATES: The amended Authorization is effective as of November 19, 2009.

ADDRESSES: Submit written requests for single copies of the EUA to the Office of Counterterrorism and Emerging Threats (HF-29), Food and Drug Administration, 5600 Fishers Lane, rm. 14C-26, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your request or include a fax number to which the Authorization may be sent. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the Authorization.

FOR FURTHER INFORMATION CONTACT: RADM Boris Lushniak, Office of Counterterrorism and Emerging Threats (HF-29), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4067.

SUPPLEMENTARY INFORMATION:

I. Amendment to the October 23, 2009, Authorization for Peramivir IV

On April 26, 2009, under section 564(b)(1)(C) of the act (21 U.S.C. 360bbb-3(b)(1)(C)), the Acting Secretary of Health and Human Services determined that a public health emergency exists involving Swine Influenza A (now known as 2009 H1N1 Influenza A, or 2009 H1N1 flu) that affects, or has the significant potential to affect, national security. The determination of emergency has been renewed. On October 20, 2009, under section 564(b) of the act, and on the basis of such determination, the Secretary declared an emergency justifying the authorization of the emergency use of the antiviral peramivir, accompanied by emergency use information subject to the terms of any authorization issued under 21 U.S.C. 360bbb-3(a). On October 23, 2009, in response to a request from CDC,

FDA issued an EUA for the emergency use of the unapproved drug peramivir administered intravenously. On November 2, 2009, notice of the determination and declaration was published in the **Federal Register** (74 FR 56640, November 2, 2009), as was the notice of the Authorization (74 FR 56644, November 2, 2009). In response to inquiries about dosing of Peramivir IV in certain patients with severe renal impairment, including those who require continuous renal replacement therapy or hemodialysis, on November 19, 2009, FDA amended the Authorization letter to amend the Fact Sheet for Health Care Providers to provide additional clarification regarding the dosing recommendations for IV peramivir and reissued the Authorization letter in its entirety. The amended dosing recommendations are provided in the amended authorized version of the Fact Sheet for Health Care Providers.

II. Electronic Access

An electronic version of this notice and the full text of the Authorization are available on the Internet at <http://www.regulations.gov>.

III. The Authorization

Having concluded that the criteria for issuance of the Authorization under section 564(c) of the act were met, on October 23, 2009, FDA authorized the emergency use of the unapproved drug peramivir administered intravenously for treatment of 2009 H1N1 influenza virus in certain adult and pediatric patients. The letter of Authorization in its entirety (not including the amended authorized version of the Fact Sheet for Health Care Providers), as amended on November 19, 2009, follows: