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Guidance on the Conduct and Review of Studies to Support New Animal Drug Development during the COVID-19 Public Health Emergency

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Guidance for Industry

April 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or the Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number FDA-2020-D-1140 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "Coronavirus Disease 2019 (COVID-19)," *available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders, and the FDA webpage titled "Search for FDA Guidance Documents," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents, and the Center for Veterinary Medicine webpage titled "Guidance for Industry," *available at* https://www.fda.gov/animal-veterinary/guidance-regulations/guidance-industry. You may also send an e-mail request to AskCVM@fda.hhs.gov to receive a copy of the guidance. Please include the document number FDA-2020-D-1140 and complete title of the guidance in the request.

Questions

For questions about this document, contact AskCVM@fda.hhs.gov.

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This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. Introduction

The Food and Drug Administration ("FDA" or "Agency") plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 ("COVID-19") pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

FDA is issuing this guidance to provide recommendations for sponsors conducting studies to support new animal drug development to help ensure the safety of animals, their owners, and study personnel, maintain compliance with good laboratory practice regulations and good clinical practice, and maintain the scientific integrity of the data during the COVID-19 pandemic.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Department of Health and Human Services (HHS), including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Services (PHS) Act.

Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020 *available at* https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (*see* section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a

topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "SARS-CoV-2" and the disease it causes has been named Coronavirus Disease 2019, or COVID-19. On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[1] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[2]

The Center for Veterinary Medicine ("CVM") is aware that the COVID-19 pandemic may have an impact on studies conducted to support new animal drug development. Many of the challenges noted in FDA's Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic, issued in March 2020 (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic), may arise during the conduct of studies intended to support the approval of new animal drugs. Therefore, we believe the general principles outlined in that guidance document may be applied to studies conducted to support animal drug development. In the discussion below, we provide specific recommendations as to how these principles may be applied to studies conducted to support new animal drug development to ensure the safety of animals, their owners, and study personnel, maintain compliance with good laboratory practice regulations and good clinical practice, and maintain the scientific integrity of the data.

III. Discussion

This section includes CVM's answers to the following questions regarding the conduct of studies to support new animal drug development as well as questions regarding CVM's coordination with foreign regulatory authorities during the COVID-19 pandemic.

A. On-going studies.

Q1. What should sponsors do for ongoing studies in client-owned animals where it is not possible to bring animals to the clinic for regularly scheduled visits?

Ensuring the safety of everyone involved in the conduct of a study is paramount. This includes animal owners, investigational site personnel for clinical trials, and study personnel for laboratory studies.

The implementation of alternative processes should be consistent with the protocol to

[1] Secretary of Health and Human Services Alex M Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020), *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx).

[2] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.

the extent possible.

For individual instances where it is not possible to collect effectiveness or safety data, sponsors should document the reasons for failing to obtain such data (e.g., identifying the specific limitation imposed by the COVID-19 public health emergency leading to the inability to perform the protocol-specified assessment).[3]

Sponsors may consider amending the protocol to modify data collection methods, e.g., in-person clinic visits changed to telephone or video case evaluations and documenting the reasons for amending the protocol. For protocol deviations necessitated by the impact of the current COVID-19 pandemic, sponsors should document the specified protocol deviation and the reason for the deviation.

Protocol amendments may include modifying study procedures or adding data collection methods. We note that for longer studies, once the public health emergency is over, sponsors should re-evaluate amendments made to the protocol during this time. If questions or concerns arise about making such amendments or re-evaluating amendments made during this time, please reach out to the appropriate Office of New Animal Drug Evaluation (ONADE) review division to discuss the amendments further.

Q2. What are some considerations concerning missing data in both proof of concept studies and studies intended to support safety or substantial evidence of effectiveness due to restricted travel?

These situations will be handled on a case-by-case basis. We recommend that sponsors reach out to the appropriate ONADE review division to discuss their specific study.

Changes in study visit schedules, missed visits, or patient discontinuations may lead to missing information (e.g., for protocol-specified procedures). It will be important to capture specific information in the case report form that explains the basis of the missing data, including the relationship to COVID-19 for missing protocol-specified information (e.g., from missed study visits or study discontinuations due to the COVID-19 public health emergency).[4]

Q3. What actions should be taken to continue ongoing studies if the quality monitoring of a critical study phase is disrupted?

If planned on-site monitoring visits are no longer possible, sponsors should consider optimizing use of central and remote monitoring programs to maintain oversight of clinical sites.[5]

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[3] See FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic (March 2020) at p. 7. (https://www.fda.gov/media/136238/download)

[4] See FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic (March 2020) at p. 7. (https://www.fda.gov/media/136238/download)

[5] See FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic (March 2020) at p. 8. (https://www.fda.gov/media/136238/download)

For example, sponsors may use remote monitors and commonly available video communication applications for study monitoring purposes, as appropriate.

Q4. How will CVM address challenges posed by monitoring and quality assurance (QA) review during the in-life phase of the study, reduced enrollment, extended study enrollment period and observations by limited clinic staff?

Remote monitoring, remote study visits for animals and their owners, and remote safety assessments by clinic staff are acceptable, as appropriate, to ensure safety for everyone involved in the conduct of the study and to maintain scientific integrity of the data.

Q5. What should sponsors do if a study or enrollment in a study is paused because of the COVID-19 public health emergency?

A sponsor may determine that a study or enrollment in a study needs to be paused during the COVID-19 public health emergency. In such cases sponsors should consider how they will protect study and data integrity. For example, we recommend you ensure that identity and treatment assignment masking is maintained during the pause and that you not perform interim analyses unless specified in the protocol. Sponsors should also document any protocol amendments that may be necessary and their potential impact on the study. During this time, we recommend that sponsors notify CVM if a study is put on hold.

Q6. How can sponsors continue to interact with CVM for interactions that typically occur face-to-face, e.g., method trial demonstrations related to human food safety?

CVM plans to address these situations as they arise on a case-by-case basis. Depending on the exact nature of the interaction, CVM is open to using remote tools such as webcams and videos, when appropriate.

B. Coordination with foreign regulatory authorities.

Q7. Does CVM anticipate any delays in the review of submissions (such as protocols) that are part of a United States–Canada Regulatory Cooperation Council (RCC) simultaneous review?

Under the Regulatory Cooperation Council (RCC) agreement with Canada's Veterinary Drugs Directorate (VDD), ONADE follows our phased review timelines. When sponsors submit protocols to VDD for review, VDD aligns with CVM's timelines to the extent possible. Currently, we do not anticipate any delays in RCC projects.

Q8. Will coordination with European authorities continue during the COVID-19 pandemic?

CVM plans to continue its quarterly meetings with the European Medicines Agency (EMA) as scheduled and maintain our other communications with EMA as well.