Letter to Sponsors, Applicants and Regulated Entities

June 6, 2023

The Coronavirus Disease 2019 (COVID-19) public health emergency (PHE) declared under section 319 of the Public Health Service Act expired on May 11, 2023. Additional HHS resources on the transition are available. This letter provides updated information from the previous letter of June 9, 2022, to assist sponsors, applicants, and other CBER-regulated entities as FDA's Center for Biologics Evaluation and Research (CBER) transitions back to normal operations in calendar year 2023.

CBER took the steps described in previous letters posted on the Center's website to prioritize work that advanced the nation's public health response during the national emergency. These steps sought to address the impact of COVID-19 on day-to-day operations in CBER and for industry, while ensuring that government and private sector efforts to respond to the public health emergency (PHE) received the highest priority.

The impact of COVID-19 on CBER during the PHE was unprecedented and placed tremendous burdens on product development, approval, and surveillance functions. CBER received 233 INDs/IDEs, 6,336 Expanded Access INDs, and held 188 formal meetings focusing on COVID-19 products. To date, CBER has approved 3 BLA/BLA supplements, authorized 5 EUAs (and multiple EUA revisions), and allowed over 6000 expanded access treatment requests aimed at preventing or treating COVID-19 to proceed. See Biological Approvals by Year.

While CBER's COVID-19 workload has been greatly reduced in most areas, there remains significantly increased regulatory work related to COVID-19 vaccines. In addition, CBER's non-COVID-19 vaccine review workload continues to be substantial. Therefore, for the remainder of this calendar year, CBER will continue prioritizing resources for COVID-19 vaccine regulatory work over non-COVID-19 vaccine work, as needed, to meet public health needs, including to protect against new variants.

For additional information on COVID-19 see Coronavirus Disease 2019 (COVID-19).

CBER Meetings

At the beginning of the COVID-19 PHE, CBER leveraged technology to convert all applicant and sponsor in-person meetings to virtual meetings. Beginning on February 13, 2023, CBER restarted accepting requests for certain in-person, Face-to-Face (FTF) industry PDUFA meetings (with a hybrid component). CBER will transition in phases to accepting requests for

in-person meetings for all types of FTF formal meetings. Sponsors and applicants should monitor the Formal Meetings for CBER-Regulated Products Webpage for updates regarding in-person meetings.

FDA Guidance

In the Federal Register of March 2023, FDA published a notice addressing the Agency's COVID-19-related guidance documents, including which of those documents would no longer be in effect after the expiration of the COVID-19 PHE, and which of those guidance documents FDA was revising to temporarily continue in effect. Please see COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders for further information.

Processing of Incoming Documents and CBER Responses

The CBER Document Control Center (DCC) processes regulatory applications and submissions regardless of format or method of delivery.

Commercial applicants and sponsors must be submitted in the standard eCTD format using the Electronic Submission Gateway (ESG) as described in guidance for industry, Providing Regulatory Submission in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications. Questions about the eCTD format or the ESG can be submitted to esubpred@fda.hhs.gov.

For routine submissions that are not subject to or are exempted from the eCTD requirements, applicants have the option of submitting via email. The FDA has a 150MB size limit for email/attachments. In some instances, larger email submissions can be serialized in several emails (i.e., 1 of 2, 2 of 2).

CBER prefers that submissions not subject to or exempted from the electronic submission requirements under section 745A of the FD&C Act as described in the 745(A) binding guidance and CBER Applications Submissions Guidance be sent in the following manner (in order of preference):

- FDA Electronic Submission Gateway
- CBER submission email box (150MB max): CBERDCC_eMailSub@fda.hhs.gov
- Electronic media (USB drive, DVD/CD) with no paper components
- Paper submissions

Paper and physical media submission should be sent to:

U.S. Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71, G112
Silver Spring, MD 20993-0002

Regulatory communications from CBER to sponsors and applicants will generally be sent via secure e-mail. To establish secure email, please follow the instructions in SOPP 8119 *Use of Email for Regulatory Communications,* Appendix A.

As always, the following can be sent to CBER via non-secure email: Requests for Individual Patient INDs under Expanded Access, including for emergency use; Compassionate Use IDEs; Requests for EUAs and Pre-EUAs; Emergency requests for alternative procedures or exceptions under 21 CFR 640.120; and requests for information that are general in nature. For more information about requesting expanded access for medical devices, see Expanded Access for Medical Devices | FDA.

Extension of Response Due Dates for Device Marketing Applications Currently on Hold

FDA announced in the Federal Register on June 7, 2022, the withdrawal of the guidance document entitled, "Effects of the COVID-19 Public Health Emergency on Formal Meetings and User Fee Applications for Medical Devices—Questions and Answers (Revised)," which was issued in June 2020 (and updated December 2020). This guidance described FDA's policy on applicant response due dates for marketing submissions that were on hold, recognizing that applicants might face challenges in meeting their applicable response dates due to the impact of COVID-19. FDA withdrew this guidance on July 7, 2022. As stated in the withdrawal notice, for submissions or applications that receive a major deficiency letter for PMA and HDE applications or additional information letters for 510(k)s and De Novo requests prior to July 7, 2022, FDA does not intend to consider the submission or application to be withdrawn for an additional 180 days beyond the relevant response date. For submissions or applications that receive a major deficiency letter or additional information letter after July 7, 2022, FDA will generally consider the application or submission to be withdrawn if a complete response is not received by the relevant response date identified in that letter.

FDA is planning to retain with appropriate changes to guidance document, Supplements for Approved Premarket Approval (PMA) or Humanitarian Device Exemption (HDE) Submissions

During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised) | FDA, after expiration of the COVID-19 PHE declaration. During that time, FDA plans to further revise this guidance with any appropriate changes based on comments received and the Agency's experience with implementation. Please monitor the FDA website for further information.

Conduct of Clinical Trials involving Medical Products

Recognizing that the COVID-19 pandemic may impact the conduct of clinical trials and could result in protocol modifications or unavoidable protocol deviations, FDA issued Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency to assist sponsors. This guidance is intended to remain in effect until November 7, 2023, unless superseded by a revised final guidance before that date. For further information, refer to the Federal Register Notice of March 13, 2023. Questions on specific clinical trials should be directed to the assigned product office.

Postmarket and Compliance Activities

In response to the ongoing COVID-19 pandemic, CBER paused certain lot release activities beginning on March 23, 2020, and was not receiving biological product samples or protocols in physical form (paper or CD-ROM) until further notice. CBER is resuming normal Lot Release operations in 2023. Applicants should monitor the CBER Lot Release website for updates regarding lot release activities.

How to submit an Inquiry for a Single Patient IND

FDA is committed to increasing awareness and facilitating expanded access to investigational drugs for use in patients with serious or immediately life-threatening COVID-19. For additional information on gaining access to investigational drugs please see Expanded Access.

Emergency Use Authorization

The ending of the PHE will not impact FDA's ability to authorize devices (including tests), treatments or vaccines for emergency use. Emergency Use Authorizations (EUAs) for products will remain in effect until the relevant EUA declaration is terminated or the EUA is revoked, and the agency may continue to issue new EUAs going forward when criteria for issuance are met. For questions on the EUA process, please contact CBEREUA@fda.hhs.gov.

If you have any questions about this communication, please contact the Office of

Communication, Outreach and Development via email at Industry.Biologics@fda.hhs.gov, 240-402-8010, or 800-835-4709.

Sincerely,

/s/

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