



Our STN: BL 125842/0

**COMPLETE RESPONSE**

JULY 9, 2025

Capricor, Inc.  
Attention: Margaret Kayo, PhD, MBA  
10865 Road to the Cure, Suite 150  
San Diego, CA 92121

Dear Dr. Kayo:

Please refer to your Biologics License Application (b) (4)  
for deramiocele, (b) (4)

We have completed our review of all the submissions you have made relating to this BLA, with the exception of the information in the amendments submitted and received on (b) (4), as noted below. After our complete review, we have concluded that we cannot grant final approval because of the deficiencies outlined below.

#### Clinical and Biostatistics

1. Your application provides data from the HOPE-2 and HOPE-2-OLE studies as the proposed primary and supportive evidence of effectiveness, respectively, for your product, deramiocele. The HOPE-2 study failed to demonstrate efficacy for its prespecified primary efficacy endpoint, which was change from baseline to Month 12 in the mid-level (elbow) dimension of the Performance of Upper Limb version 1.2 (PUL 1.2), a neuromuscular outcome assessment. Additionally, HOPE-2 failed to demonstrate efficacy on its prespecified secondary endpoints. To support your proposed indication for treatment of cardiomyopathy in patients with Duchenne muscular dystrophy (DMD), you have presented post hoc analyses of HOPE-2 and HOPE-2-OLE. However, as outlined below, these post hoc analyses are not sufficient to provide substantial evidence of effectiveness to support approval of deramiocele.
  - a. As stated in your response to an FDA information request (dated (b) (4)), the HOPE-2 study was intended to evaluate the effectiveness of deramiocele on neuromuscular function and was not designed to assess effectiveness for the treatment of cardiomyopathy in patients with DMD. Thus, HOPE-2 was not an adequate and well-controlled study with a clear statement of the objectives of the investigation and without sufficient

prespecified collection of essential baseline clinical data to assess effectiveness for the treatment of cardiomyopathy in patients with DMD.

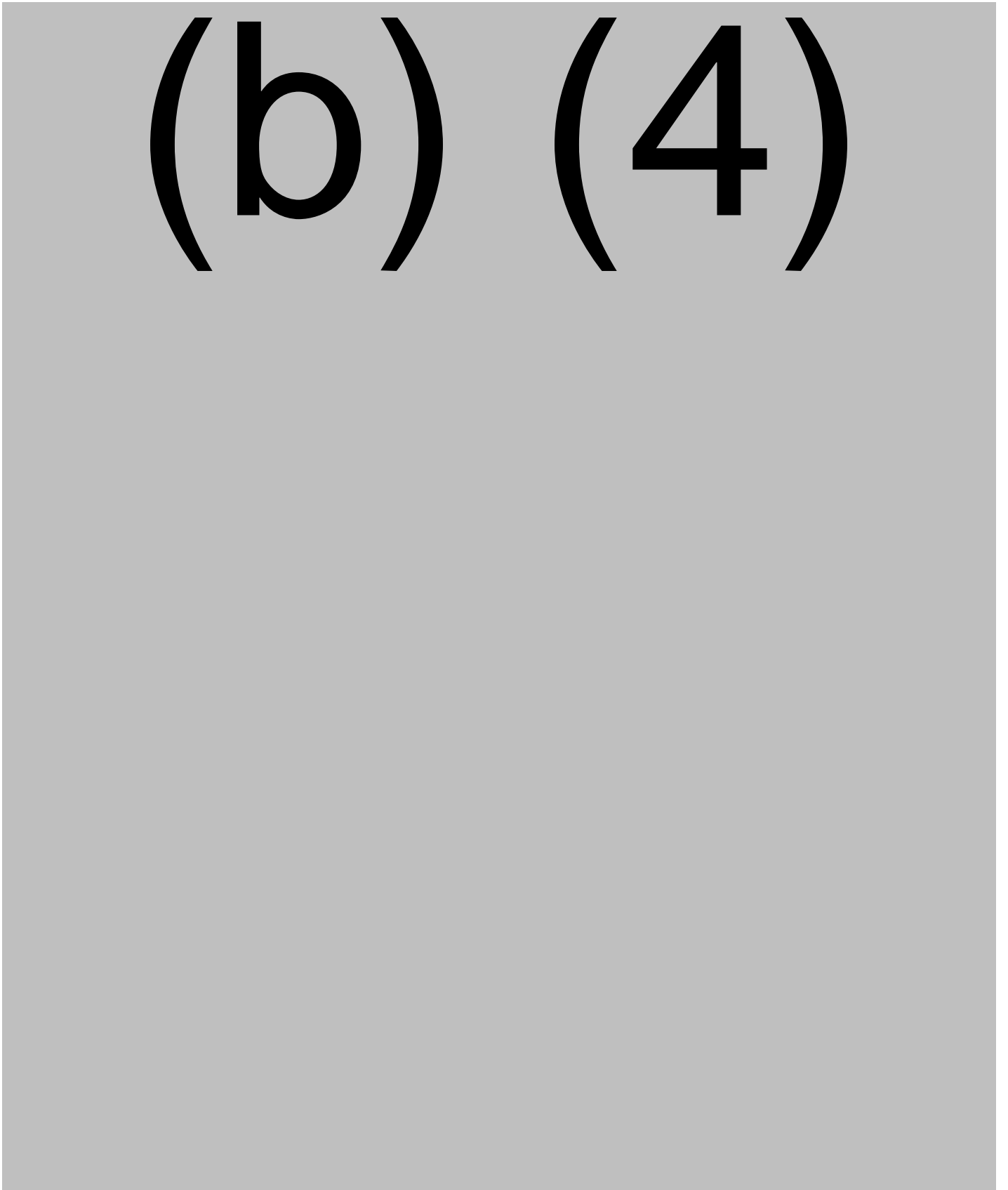
- b. The data submitted in this BLA to support the proposed indication include 50 secondary and exploratory endpoints, including post hoc analyses of 26 endpoints of cardiac MRI assessments. These 50 secondary and exploratory endpoints were not prespecified for hypothesis testing, and no prespecified multiplicity adjustment strategy was employed for control of the overall Type 1 error rate. As such, these analyses are exploratory and hypothesis-generating only and cannot provide evidence of effectiveness. No overall consistency in treatment effect was evident across a large number of exploratory cardiac endpoints in the primary HOPE-2 study, suggesting that the few nominally significant findings could be spurious. Similarly, the post hoc and exploratory analyses of cardiac function from the nonrandomized HOPE-2-OLE study are subject to potential unmeasured confounding and inflation of Type 1 error.

The Federal Food, Drug, and Cosmetic Act (FD&C Act), Section 505(d), 21 Code of Federal Regulations (CFR) § 314.126, and Section 351 of the Public Health Service Act (PHS Act) require substantial evidence of effectiveness from adequate and well-controlled studies to support a marketing application of a drug or biological product. Your BLA does not meet the statutory requirement for substantial evidence of effectiveness. If you wish to seek approval of deramiocelel for treatment of cardiomyopathy in patients with DMD, we recommend that you conduct adequate and well-controlled study(ies), whose primary objective is evaluation of cardiac outcomes in deramiocelel-treated patients with DMD cardiomyopathy, compared to a randomized, concurrent control group over an appropriate duration of follow up.

Chemistry, Manufacturing, and Controls (CMC)

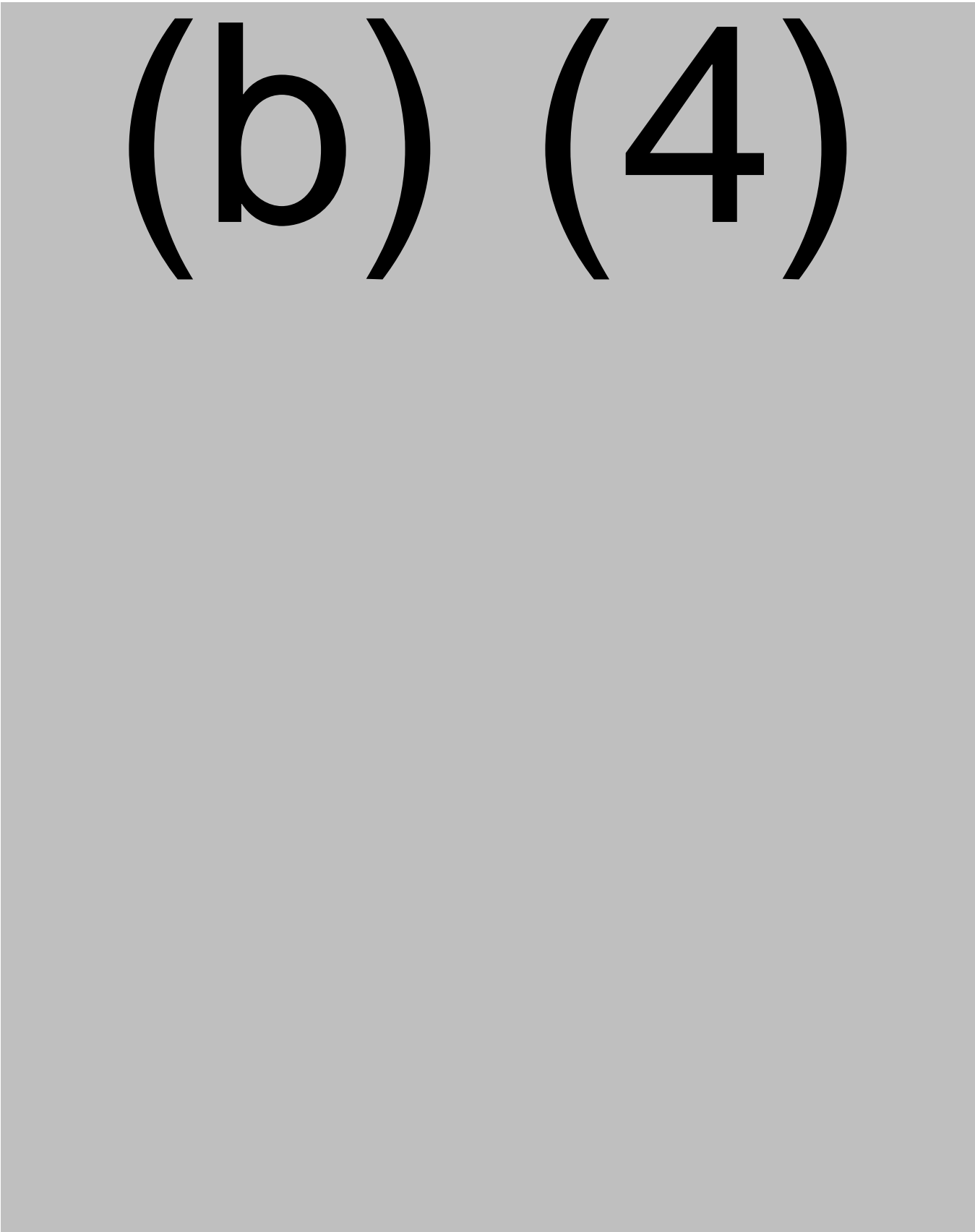
(b) (4)

(b) (4)



CMC [Facility and Equipment]

(b) (4)

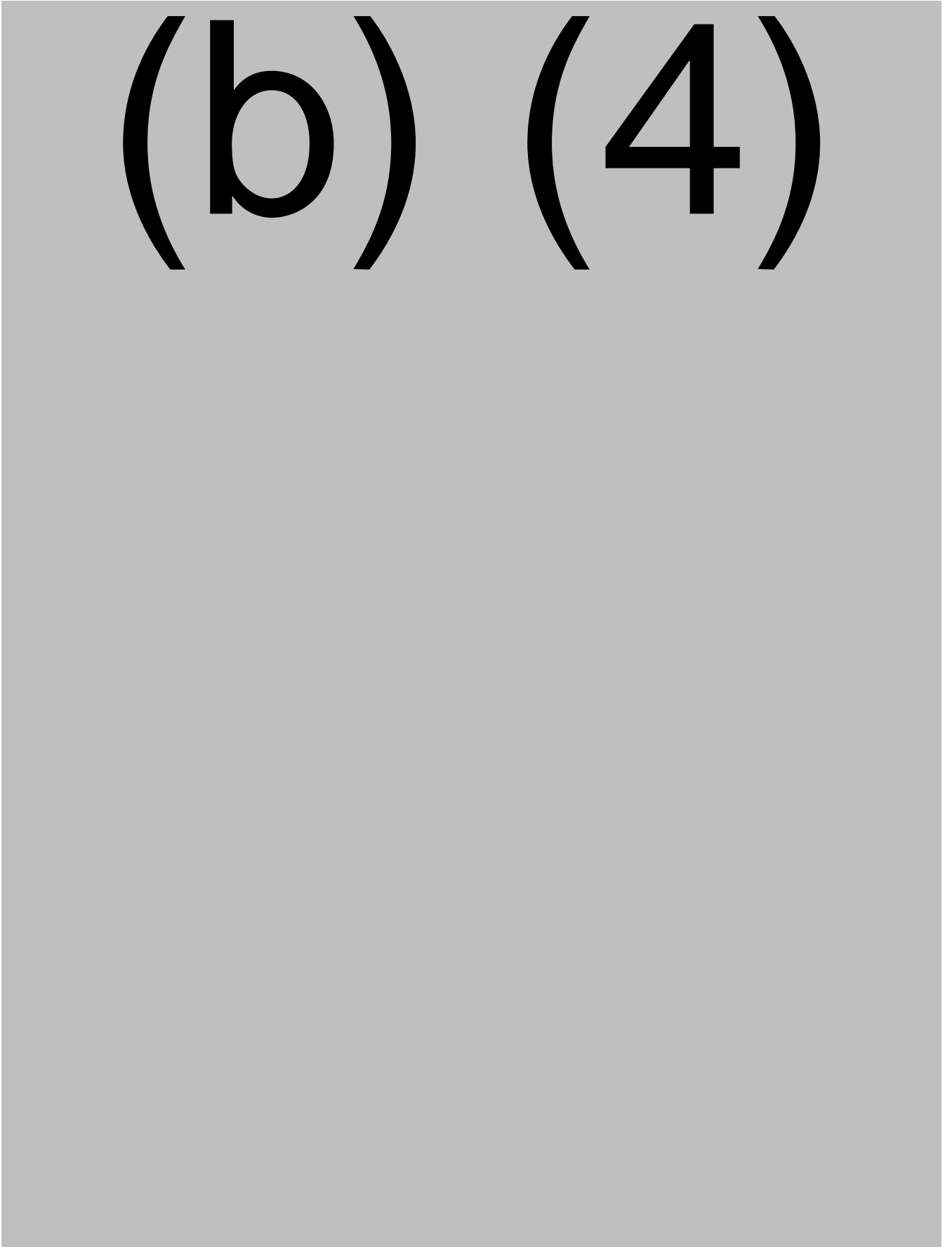


(b) (4)

ADDITIONAL COMMENTS

(b) (4)

(b) (4)



(b) (4)

13. We acknowledge receipt of your proposed labeling and anticipate conducting a detailed labeling review once the above concerns have been fully addressed.

Within one year after the date of this letter, you are required to resubmit or withdraw the application (21 CFR 601.3(b)). If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 601.3(c). You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss the steps necessary for approval.

You may request a Type A post-action meeting within 3 months of the date of this letter. Please submit your meeting request as described in the guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM590547.pdf>, and CBER's SOPP 8101.1 *Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants* at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079448.htm>.

We acknowledge receipt of your amendments dated (b) (4). Please be aware that we have stopped the review clock with the issuance of this letter. We will reset and start the review clock when we receive your complete response. You may cross reference applicable sections of the amendments dated (b) (4) in your complete response to this letter, and we will review those sections as a part of your complete response.

If you have any questions regarding the above, please contact the (b) (4)

Sincerely,

(b) (4)

Center for Biologics Evaluation and Research