BLA 761438

COMPLETE RESPONSE

Swedish Orphan Biovitrum AB (publ)
Attention: Bao Le
US Regulatory Lead, Immunology
77 4th Avenue, 3rd Floor
Waltham, MA 02451

Dear Bao Le:

Please refer to your biologics license application (BLA) dated June 27, 2025, received June 27, 2025, and your amendments, submitted under (b) (4) for sirolimus for injectable suspension; pegadricase-sogo for injection.

We also acknowledge receipt of your amendment dated May 29, 2026, which was not reviewed for this action. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY (*pegadricase-sogo*)

(b) (4)

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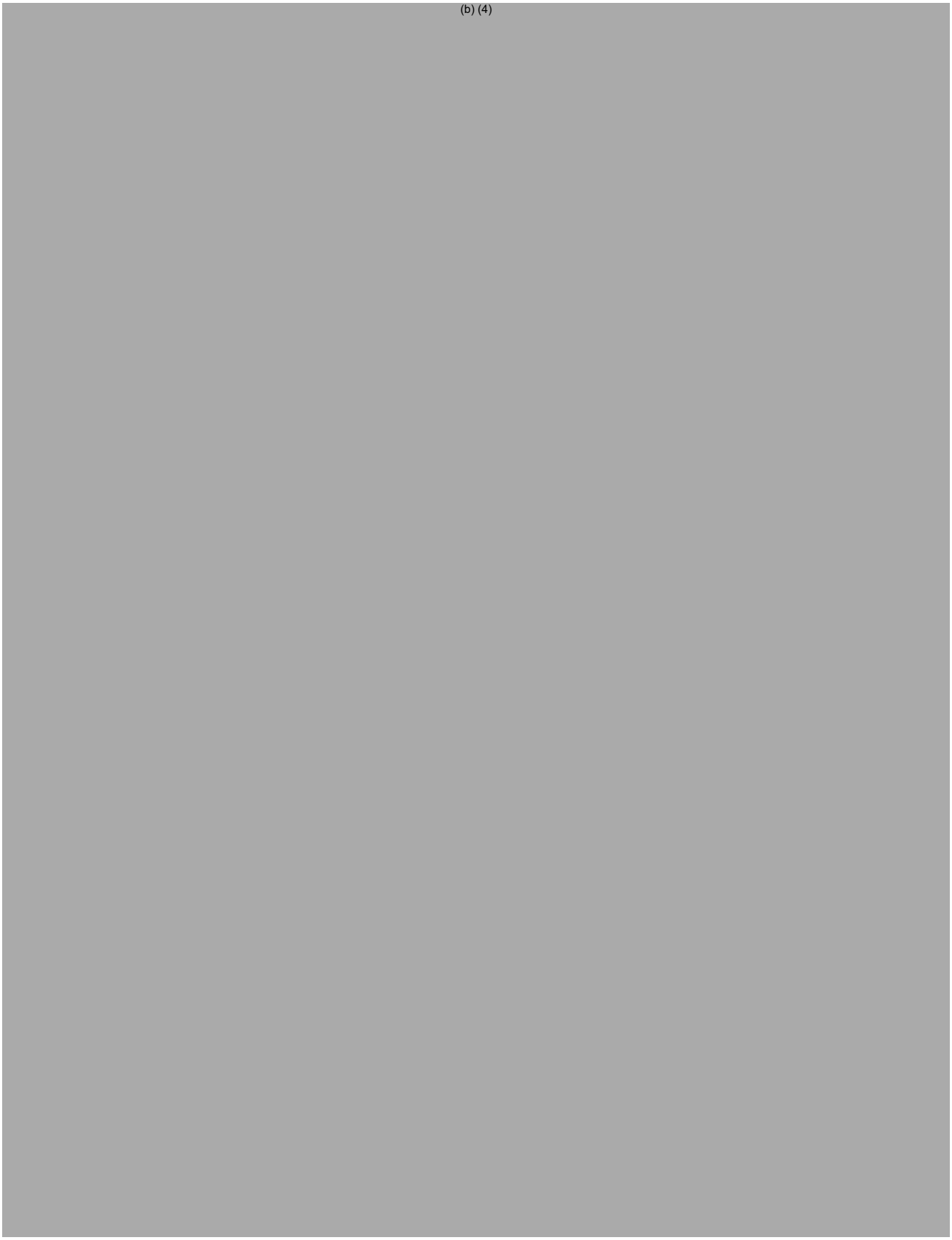

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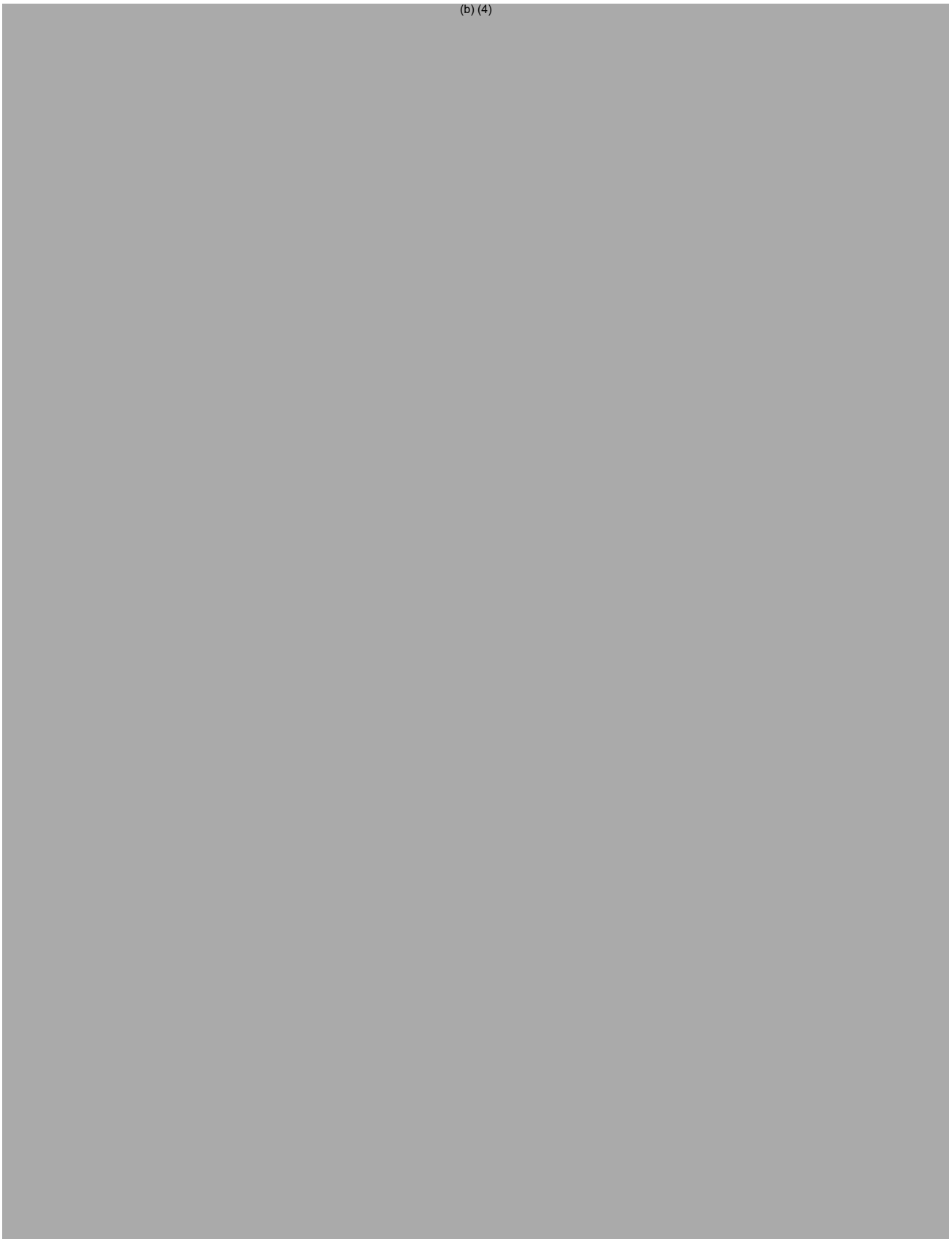

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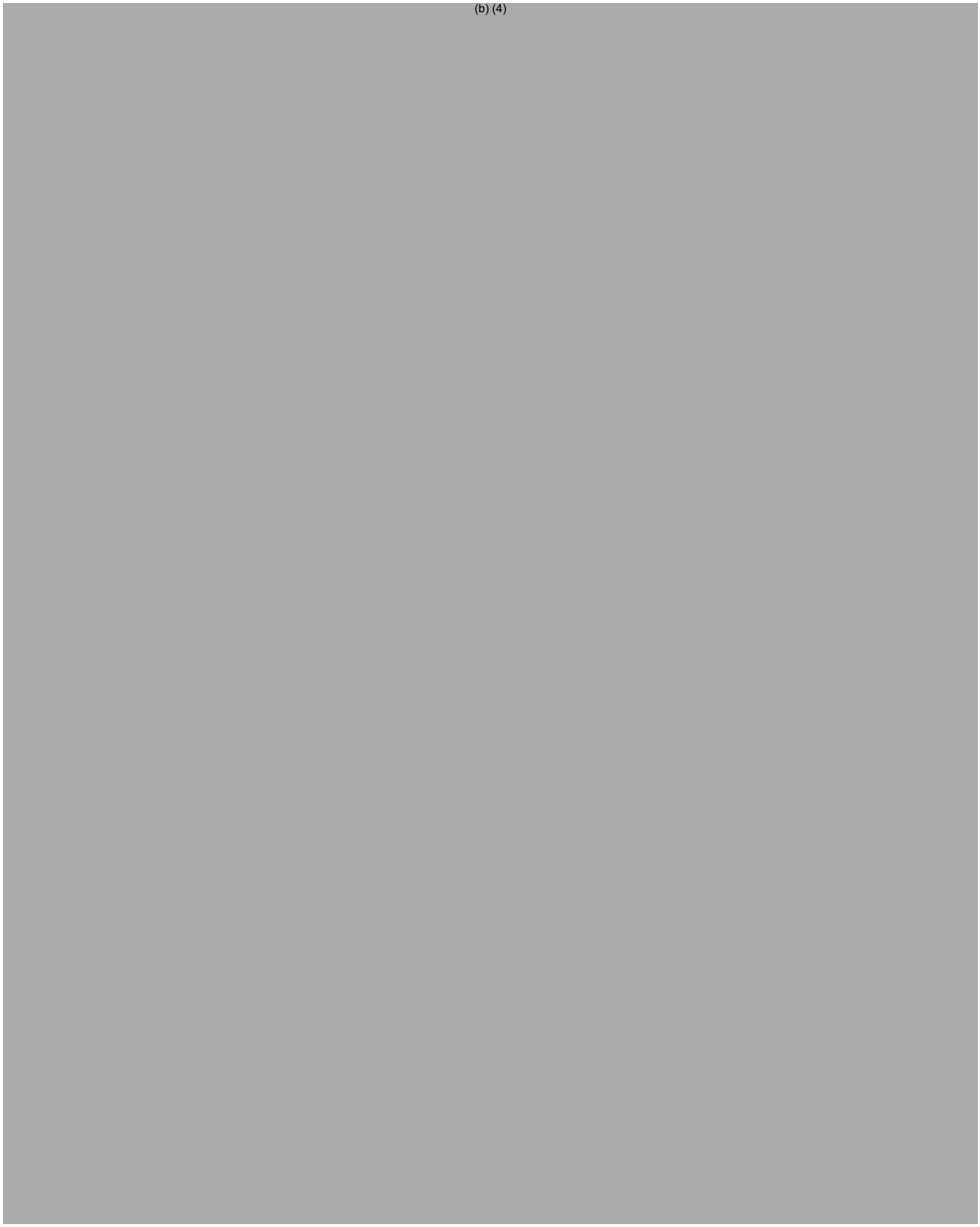

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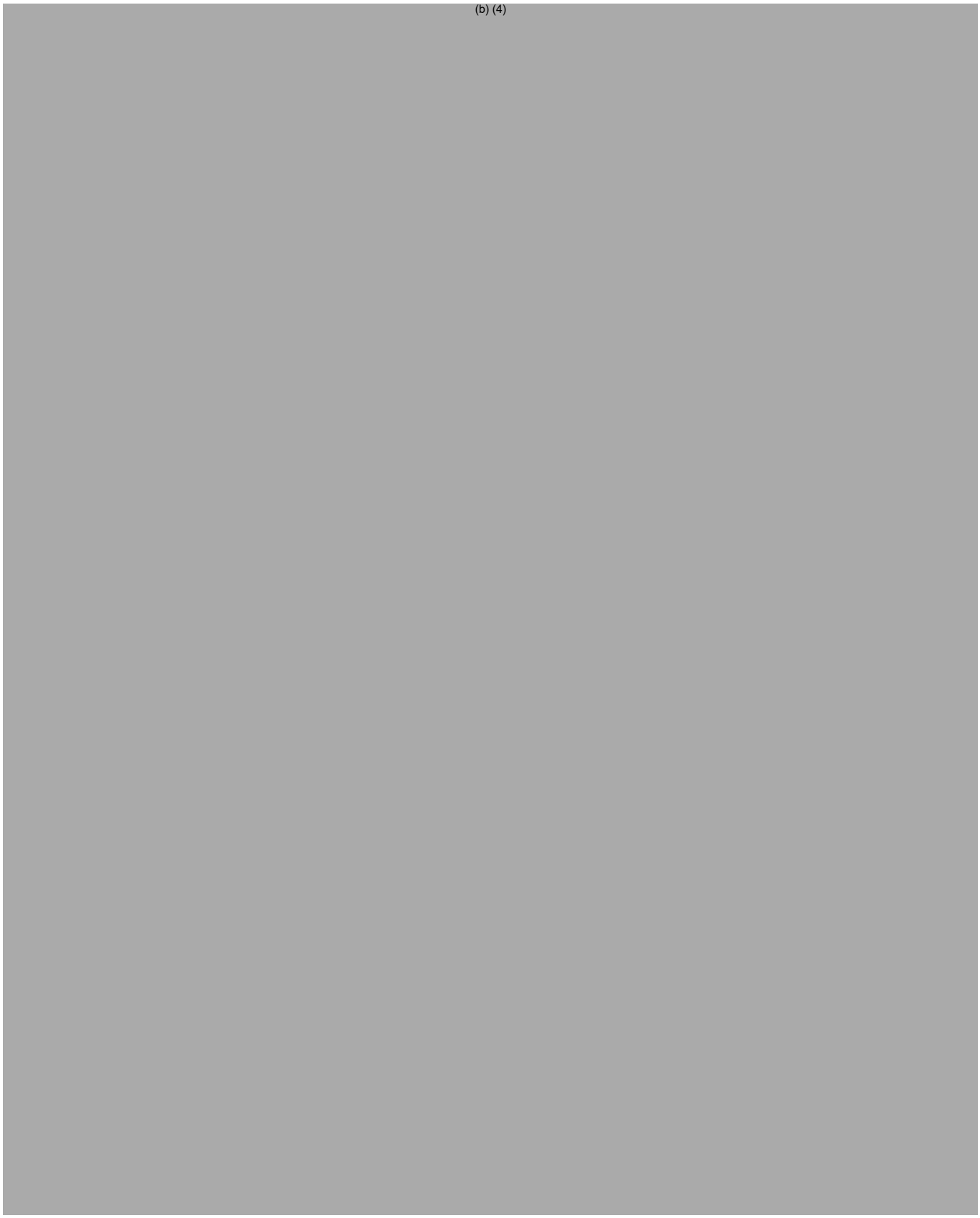

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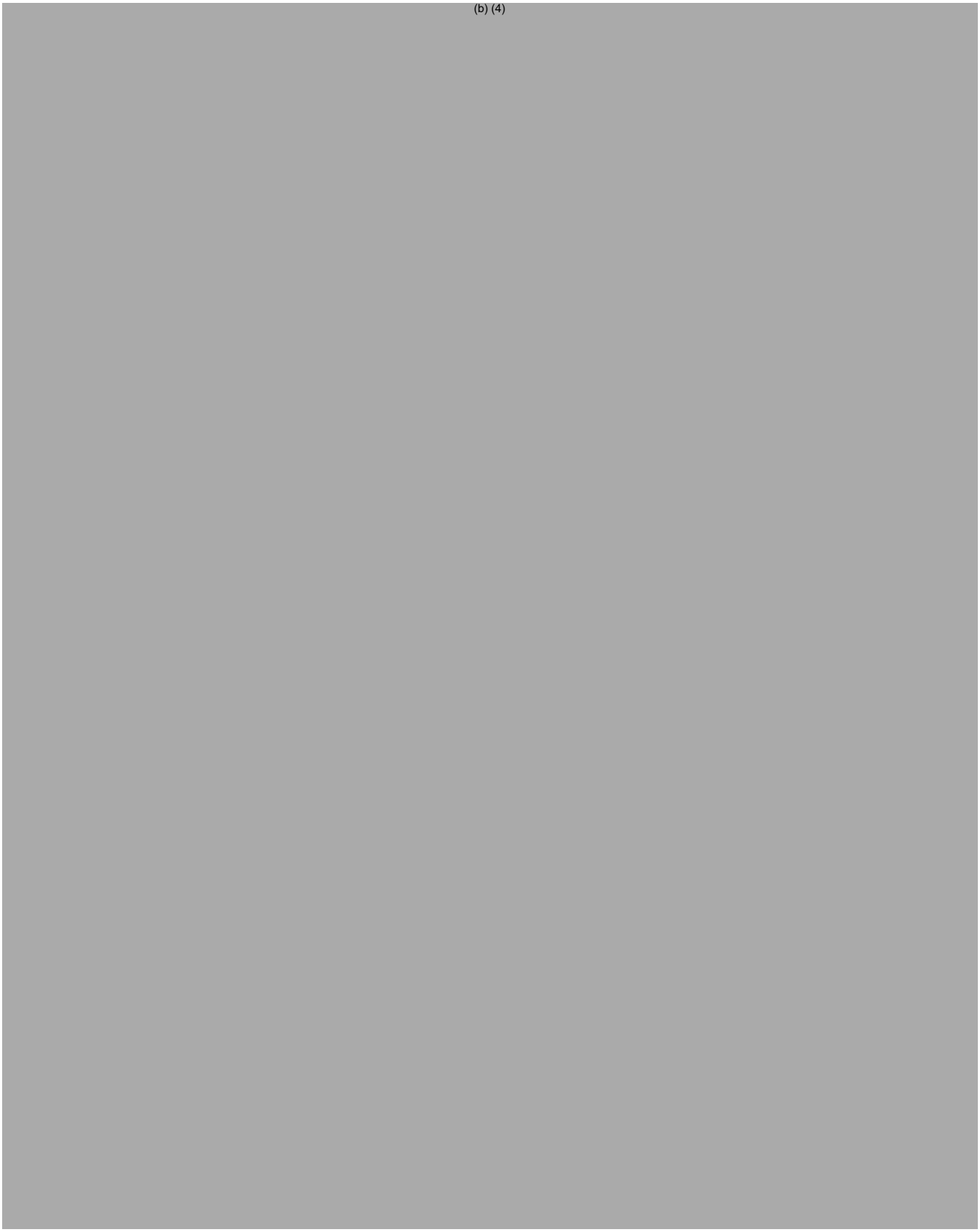

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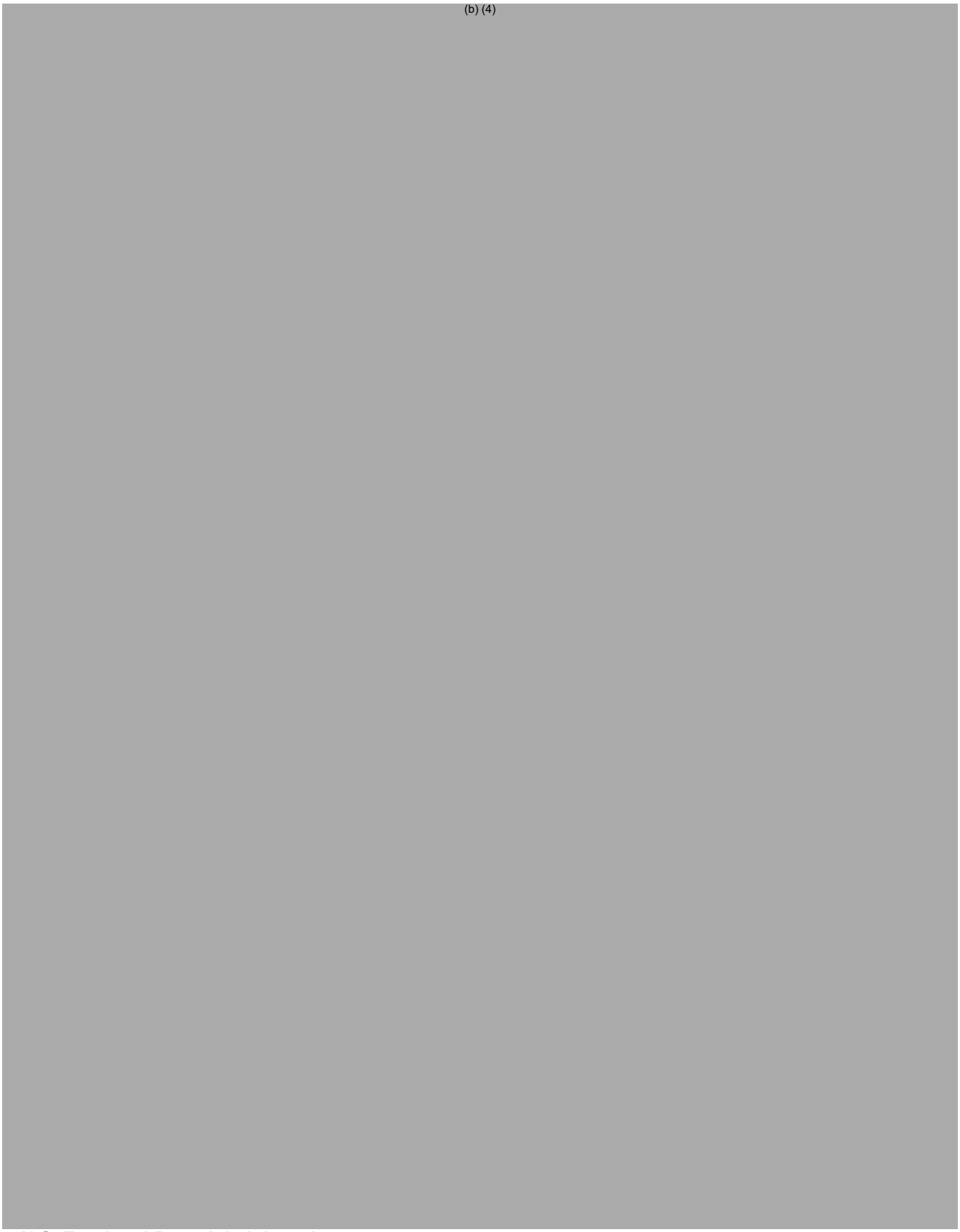

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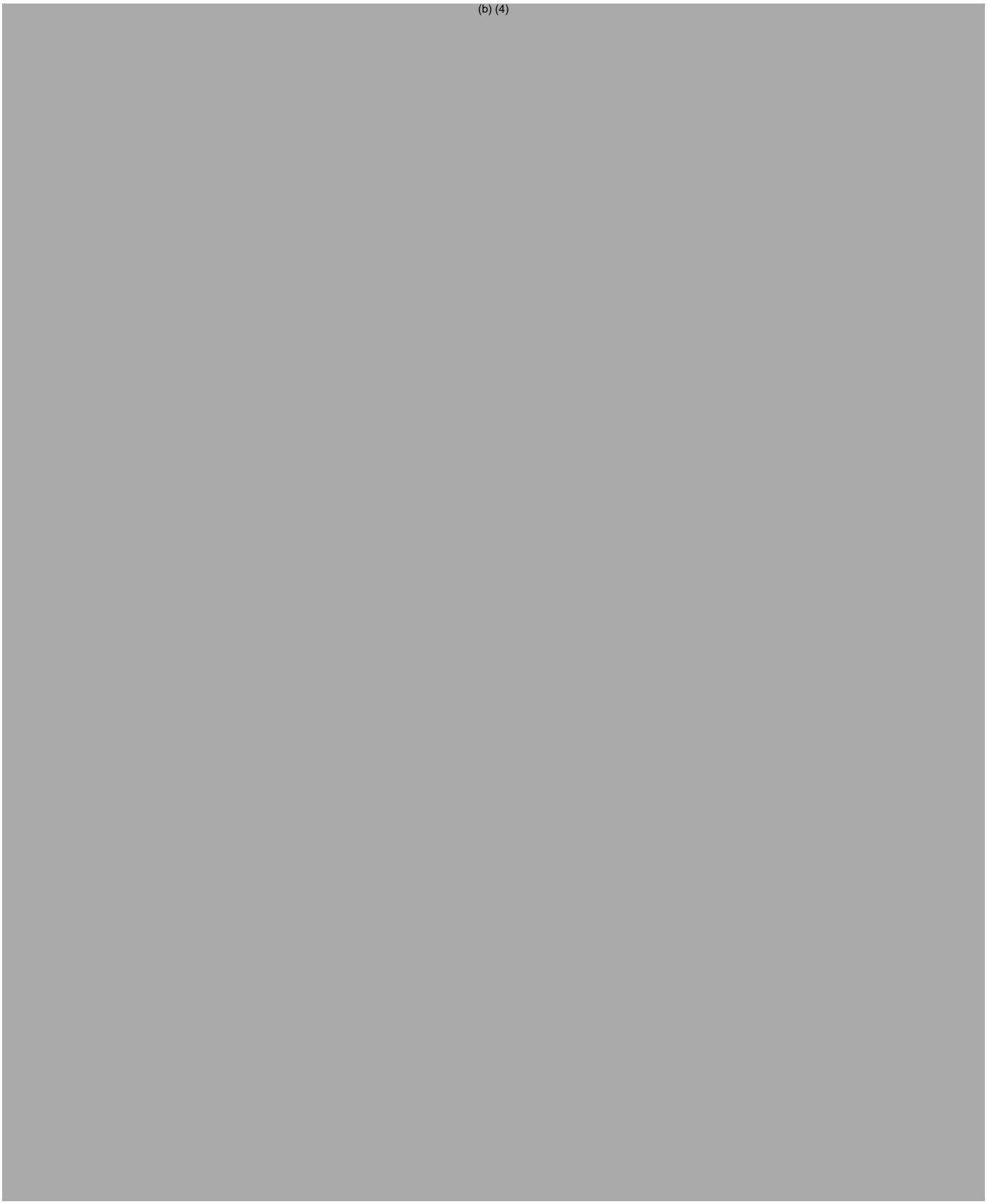

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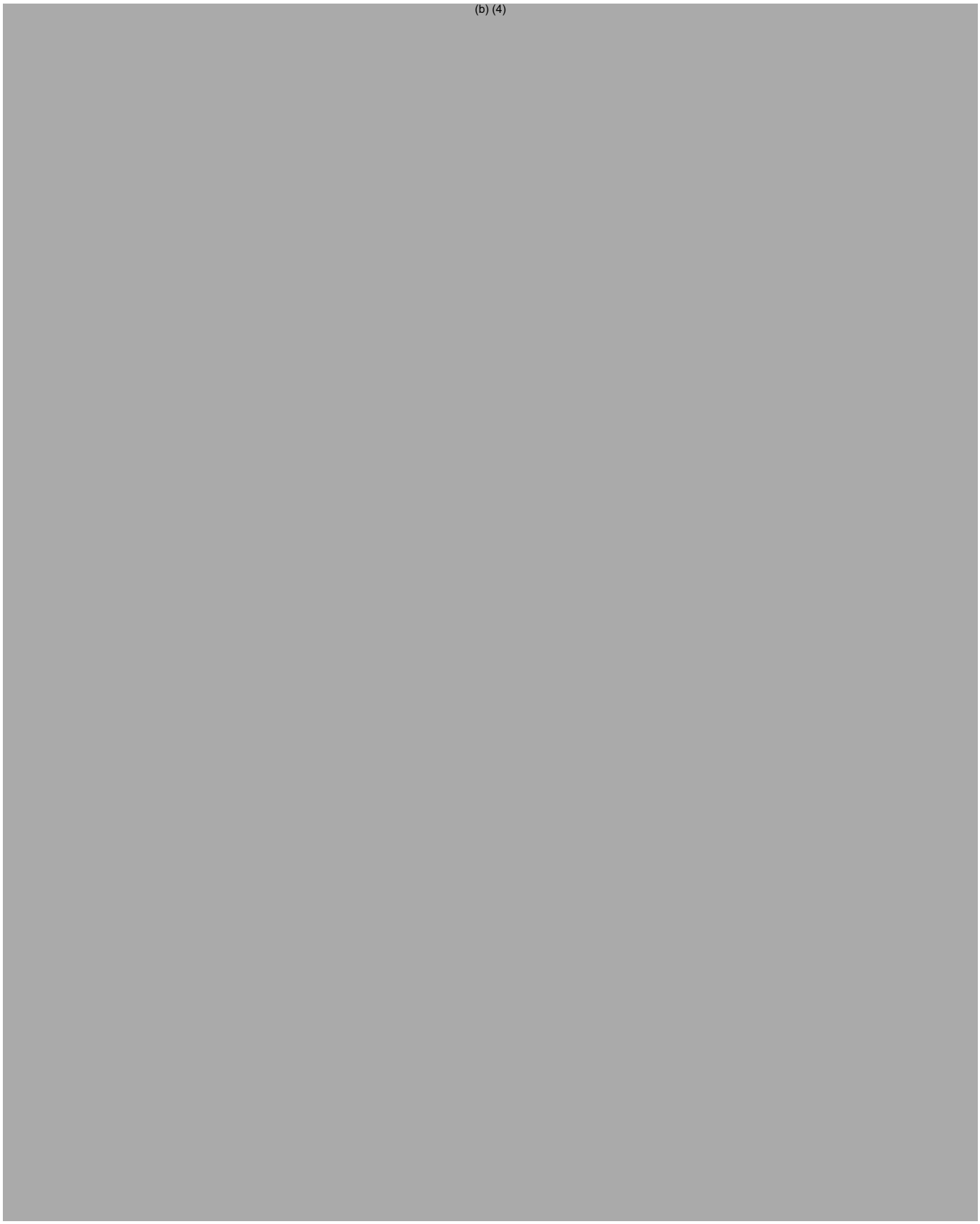

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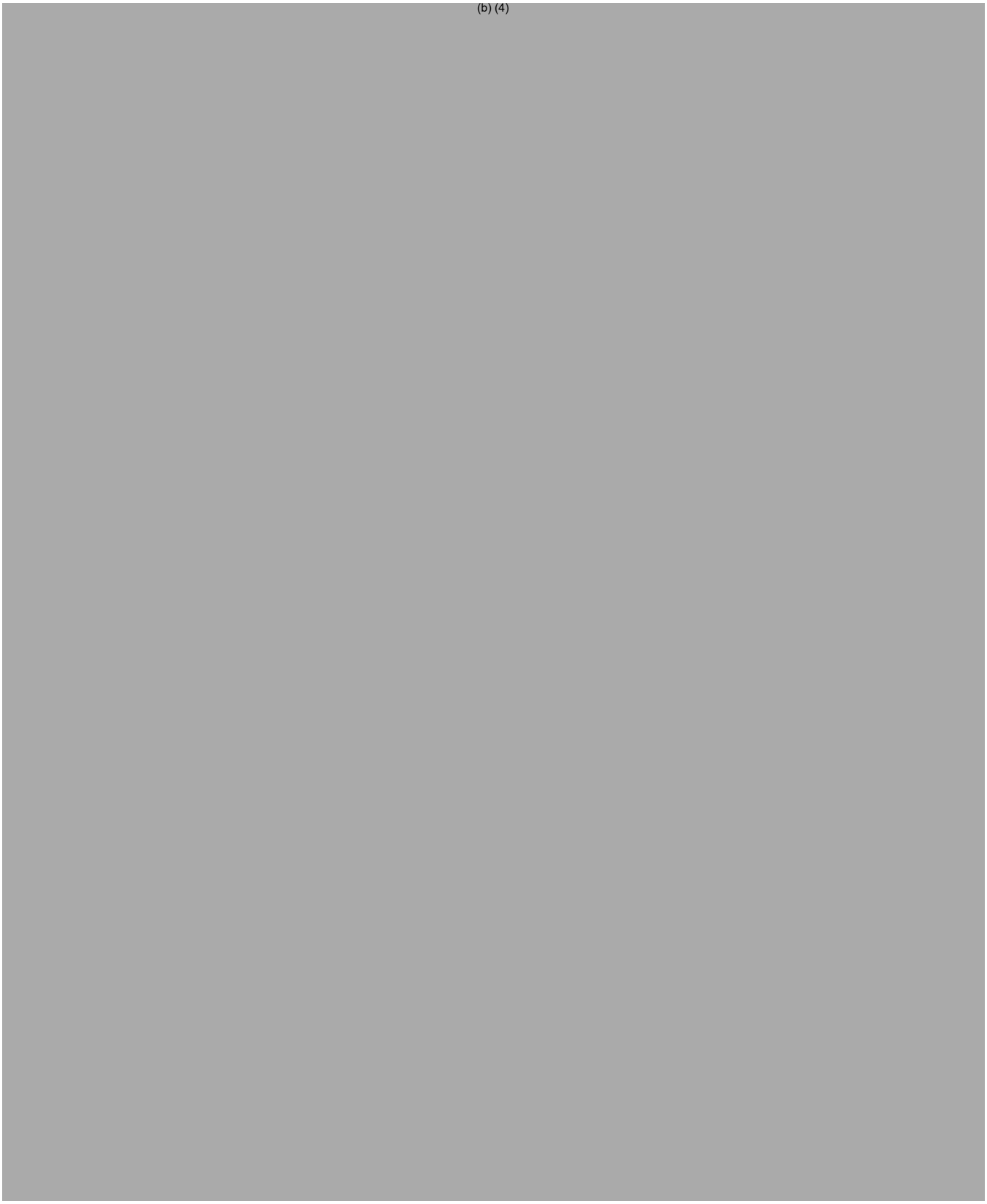

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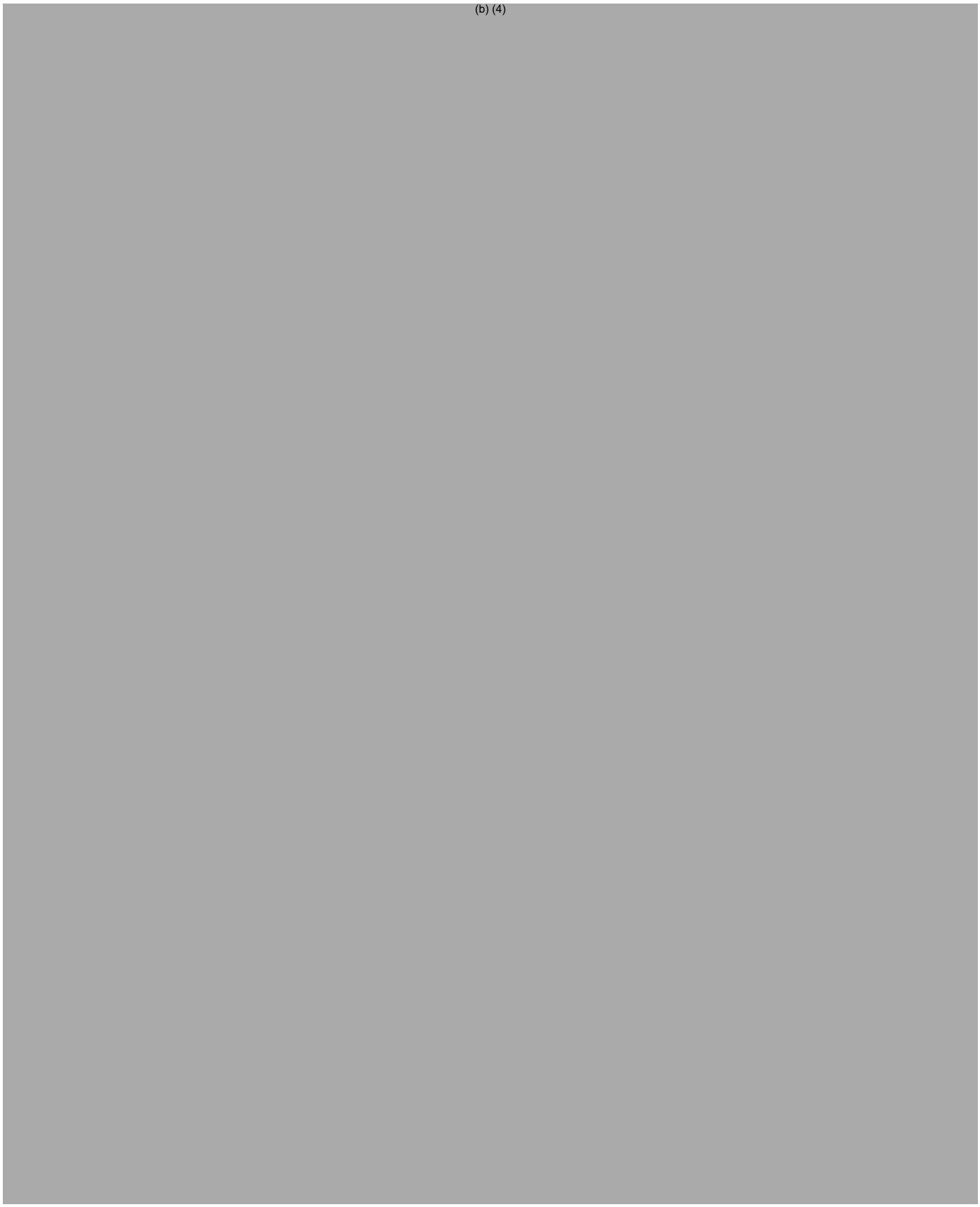

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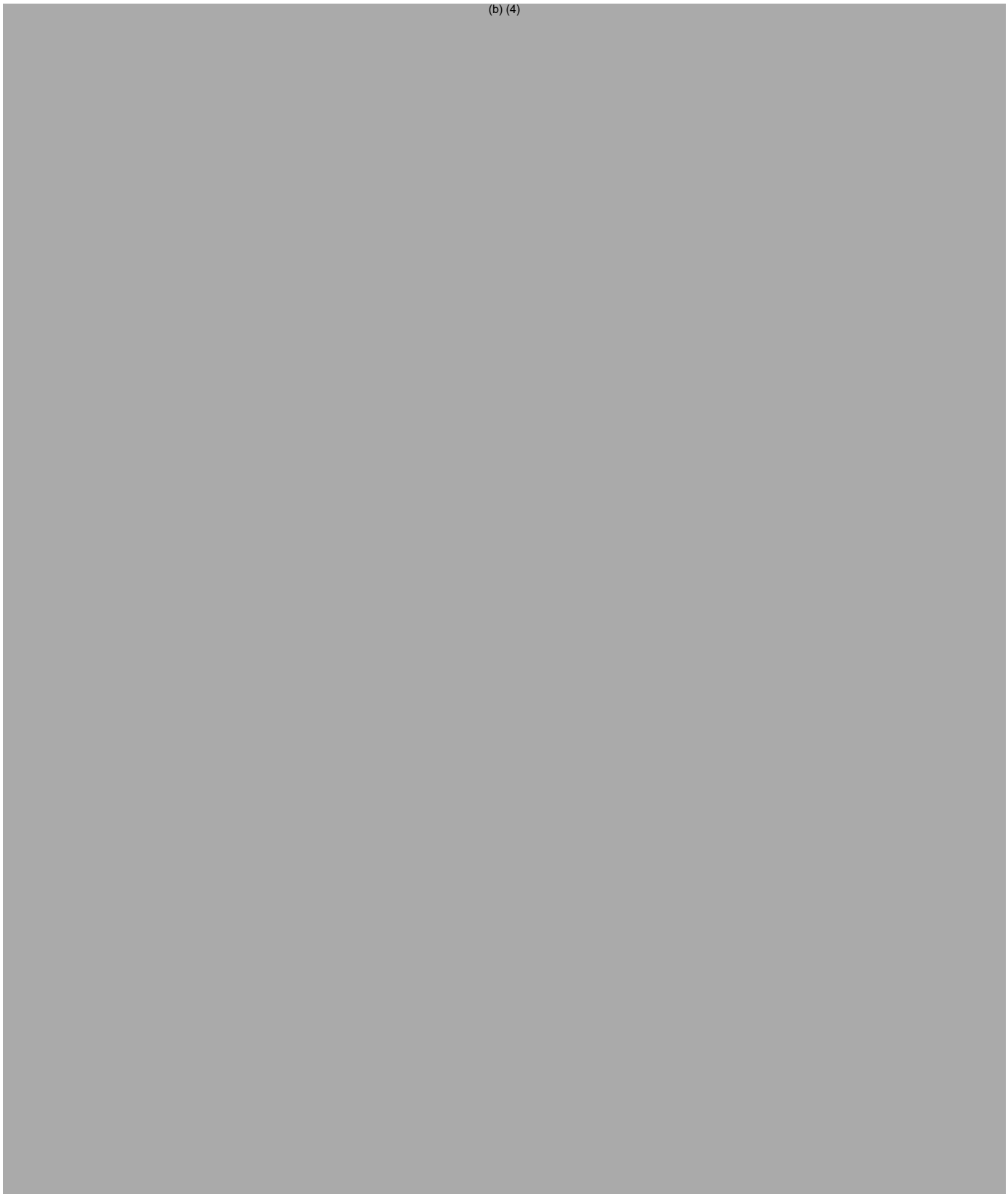

(b) (4)

FACILITY INSPECTIONS

12. Following a CGMP inspection and pre-license inspection of (b) (4), listed in this submission, FDA conveyed deficiencies to the representative of the facility. The facility should provide satisfactory responses to these deficiencies to the FDA office indicated on the FDA 483 prior to your complete response to your application. Our determination that the facility's responses are satisfactory will depend on a finding that the facility has come into compliance with CGMP and has addressed any deficiencies specific to your application. You should coordinate with the facility for timely resolution of all inspection deficiencies, as well as to determine if any deficiencies may require updates to your application. Your complete response should include the date(s) of the facility's response(s) to the FDA Form 483. Please refer to Compliance Program CP 7356.002 for guidance on post-inspection activities specific to CGMP compliance evaluation. FDA may determine that a CGMP reinspection and/or additional pre-license inspection (PLI) is needed to confirm satisfactory resolution of inspection deficiencies before this application can be approved. If both CGMP and PLI reinspection are needed, the PLI coverage will generally occur following a determination that the facility is in compliance with CGMP.

13. As part of the facility evaluation of (b) (4) a Remote Regulatory Assessment was performed. FDA identified deficiencies that were conveyed to the representative of

the facility. The facility should provide satisfactory responses to these deficiencies to the FDA office that conducted the Remote Regulatory Assessment prior to your complete response to this letter. Your complete response should include the date(s) of the facility's correspondence(s) to address these deficiencies. FDA may need to perform an onsite PLI before this application may be approved. Please be aware that we will not initiate the PLI until your complete response is received. Please work with the facility to resolve the related deficiencies and ensure the facility is ready for a PLI.

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the Prescribing Information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format as described at FDA.gov.[3]

CARTON AND CONTAINER LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate.

MEDICATION GUIDE

Add the following bolded statement or appropriate alternative to the carton and container labeling per 21 CFR 208.24(d): "**ATTENTION PHARMACIST: Each patient is required to receive the enclosed Medication Guide**."

PROPRIETARY NAME

Please refer to our correspondence dated, May 14, 2026, which addresses the proposed proprietary name, (b) (4) . This name was found conditionally acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to all of the application deficiencies that have been identified in this letter.

[1] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources
[2] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule
[3] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the drug/product under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

(2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
- Present tabulations of the new safety data combined with the original application data.
- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.
- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

(3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

(4) Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.

(5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.

(6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

(7) Provide a summary of worldwide experience on the safety of this drug/product. Include an updated estimate of use for drug/product marketed in other countries.

(8) Provide English translations of current approved foreign labeling not previously submitted.

ADDITIONAL COMMENTS

We have the following comments/recommendations that are not approvability issues; however, we recommend you address these comments prior to resubmission:

Product Microbiology (pegadricase-sogo):

(b) (4)

Product Quality (sirolimus for injectable suspension):

(b) (4)

(b) (4)

Clinical Pharmacology:

7. As communicated during the Mid-Cycle Communication, you have not conducted a clinical mass balance study for (b) (4) sirolimus, and none of the bioanalytical methods employed in any of your clinical studies were able to distinguish between (b) (4) and released sirolimus. Consequently, the impact of CYP3A4 inhibitors on each form of sirolimus are not determined, and the clinical relevance of exposure matching for total sirolimus remains unclear. Therefore, your proposed recommendations for patients receiving concomitant strong CYP3A4 inhibitors lack adequate justification.

8. We recommend conducting a hepatic impairment study to evaluate the impact of varying degrees of hepatic impairment on the pharmacokinetics (PK) of the (b) (4) sirolimus component of your proposed product to inform appropriate dosage regimens for this special population.

9. The population PK analyses for both (b) (4) sirolimus and pegadricase require further refinement and optimization on the structural models and covariate identification to improve model robustness and reliability of model application. Notably, body weight was not identified as an independent covariate on clearance for either component. Therefore, the necessity for body weight-based dosing is questionable, though no exposure dependent efficacy and safety concerns were raised.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 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 in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. 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 what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, contact (b) (4)

Sincerely,

{See appended electronic signature page}

(b) (4)

Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

(b) (4)

06/26/2026 10:05:06 AM

signing as a proxy on behalf of (b) (4)