



BLA 761357

COMPLETE RESPONSE

Gan & Lee Pharmaceuticals
C/O Gan & Lee Pharmaceuticals USA Corporation
Attention: Vanessa Brewer-Yizar
Senior Manager, Global Regulatory Affairs
520 US Highway 22 East
Suite 302
Bridgewater, NJ 08807

Dear Vanessa Brewer-Yizar

Please refer to your biologics license application (BLA) (b) (4)

for "Gan & Lee insulin lispro".

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

(b) (4)

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(b) (4)



(b) (4)



(b) (4)

FACILITY INSPECTIONS

6. Following pre-license inspection of (b) (4) listed in this application, FDA conveyed deficiencies to the representative of the facility. Your BLA resubmission should include the date of the facility's response to the FDA Form 483. The assessment of application approvability and the resolution of inspection deficiencies would be evaluated upon receipt of your BLA resubmission and may include reinspection of the facility. Please work with the facility in resolving the related deficiencies.

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 Resources² and Pregnancy and Lactation Labeling Final Rule³ 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. In addition, we encourage you to review the FDA guidance for industry *Labeling for Biosimilar Products*.

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.⁴

² <https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources>

³ <https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule>

⁴ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

CARTON AND CONTAINER LABELING

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

PROPRIETARY NAME

Please refer to correspondence dated, (b) (4), 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.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update. The safety update should include data from all nonclinical and clinical studies of the product under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile and their relevance, if any, to whether there may be clinically meaningful differences between the proposed biosimilar product and the U.S.-licensed reference product.
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 clinical studies for the proposed indication using the same format as the original BLA submission.
 - Present tabulations of the new safety data combined with the original BLA data.
 - Include tables that compare frequencies of adverse events in the original BLA with the retabulated frequencies described in the bullet above.
3. Present a re-tabulation of the reasons for premature study discontinuation by incorporating the dropouts from the newly completed studies. Describe any new trends or patterns identified.
4. Provide case report forms and narrative summaries for each subject who died during a clinical study or who did not complete a study 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 BLA data.
6. Provide updated exposure information for the clinical studies (e.g., number of subjects, person time).
7. Provide a summary of worldwide experience on the safety of this product, including adverse events known to be associated with the use of the product and immunogenicity. Include an updated estimate of use for this 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:

1.

(b) (4)

you do not have acceptance criteria proposed for most tests. This does not provide adequate quality control

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(b) (4)



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(b) (4)



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.

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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 BsUFA 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, call

(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)

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