

Complete Response Letter - Q-Pan

Our STN: **BL 125419/0**
ID Biomedical Corporation of Quebec
(dba GlaxoSmithKline Biologicals)
Attention: Michael Schwartz, Ph.D.
2301 Renaissance Boulevard,
P.O. Box 61540
King of Prussia, PA 19406-2772

Dear Dr. Schwartz:

This letter is in regard to your biologics license application (BLA) for Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted manufactured at your Quebec, Canada location and submitted under section 351 of the Public Health Service Act (42 U.S.C. 262).

We have completed our review of all the submissions you have made relating to this BLA with the exception of the information in amendments dated March 11, 2013, March 13, 2013, and March 18, 2013, as noted below. After our complete review, we have concluded that we cannot grant final approval because of the deficiencies outlined below, some of which were discussed during the conference calls between CBER and ID Biomedical Corporation of Quebec held on March 8, 2013, March 18, 2013, and March 20, 2013.

The following items pertain to the pivotal study 110464 (FLU Q-PAN-002 PRI) entitled "A Phase III, observer-blind, randomized, placebo-controlled, multi-center trial to evaluate the safety and immunogenicity of a two-dose series of monovalent A/Indonesia/5/05 (H5N1) vaccine antigen in association with AS03 adjuvant in adults aged ≥ 18 years."

1. You notified CBER on February 26, 2013, during labeling negotiations on the Prescribing Information, that ID Biomedical Corporation of Quebec inadvertently did not submit the complete study data package for FLU Q-PAN-002 with the initial BLA submitted on February 22, 2012. The 37 datasets submitted with the original BLA (referred to as D182 datasets) were not the final datasets (referred to as D364 datasets). In total, 42 D364 datasets as well as 71 Case Report Forms (eCRFs) were not submitted. Please provide the following information:

- a. The D364 datasets (42 datasets total) not included in the original BLA submission.

- b. The 71 eCRFs not included in the original BLA submission.

- c. Regarding the following datasets:

- REACCOD
- REACDOC
- WAECOD
- WCONVAC
- WDROP
- WELIG

- WGENMD
- WLYMPH
- WMEDIC
- WNOADM
- WNOVIS
- WSOLIC
- WOCEAN
- WSOLPRE
- WUNSOL
- WVITAL

i. Where applicable, please provide with each dataset a document that lists the changes between the D182 and the D364 datasets. Please include the following information in the document:

- Changes in dataset variables (i.e., variables added and deleted and the rationale for any change).
- A summary of the total number of subjects with changes from the D182 dataset to the D364 dataset in a particular category (e.g., A total of X subjects had their AE description modified. A total of X subjects had a new AE record added. A total of X subjects had an AE record deleted).
 - ii Where applicable, please provide master datasets (as SAS transport data files) that merge every record captured in the D182 and D364 datasets. Within each dataset please insert:
 - A column that captures the record outcome for each event (e.g., no change, modified from the D182 dataset, deleted from the D182 dataset, added to the D364 dataset). Please represent each outcome by a unique identifier.
 - A column that specifies, using a unique identifier, where the record is captured (i.e., the D182 dataset, the D364 dataset, or both datasets).
 - iii. If any of the summary tables (e.g., the detailed solicited AE tables in the Day 42 report and/or the unsolicited AE tables in the Day 182 report) need to be modified as a result of these changes to the safety datasets, please provide an updated final clinical summary report for Q-PAN-H5N1-002, in which you summarize the results of Days 42, 182 and 364 in a single document and identify all changes to analysis results when D364 datasets are used as compared to D182 datasets.
- Please provide source data for subjects 1666 and 5677. We are requesting these data to obtain additional information on the adverse event of “lupus” in subject 1666 and the adverse event of “vasculitis” in subject 5677, both of which were recorded in the D182 WUNSOL dataset and subsequently removed from the D364 WUNSOL dataset. Please identify by page number, within each source document, where the respective diagnoses are made, where the diagnoses are changed, and where any supporting information relevant to making and changing the diagnoses can be found.

We reserve additional comment on the proposed pharmacovigilance plan and the proposed labeling until the application is otherwise acceptable.

We stopped the review clock with the issuance of this letter. We will reset and start the review clock when we receive your complete response.

Within 10 days after the date of this letter, you should take one of the following actions: (1) amend the application; (2) notify us of your intent to file an amendment; or (3) withdraw the application.

You may request a meeting or teleconference with us to discuss the steps necessary for approval. For PDUFA products please submit your meeting request as described in our "Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants," dated May 2009. This document is available on the internet at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf> or may be requested from the Office of Communication, Outreach, and Development, at (301) 827-1800. For non-PDUFA products, please contact the regulatory project manager. For details, please also follow the instructions described in CBER's SOPP 8101.1: Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants. This document also is available on the internet at

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079448.htm>, or may be requested from the Office of Communication, Outreach, and Development.

Please be advised that, as stated in 21 CFR 601.3(c), if we do not receive your complete response within one year of the date of this letter, we may consider your failure to resubmit to be a request to withdraw the application. Reasonable requests for an extension of time in which to resubmit will be granted. However, failure to resubmit the application within the extended time period may also be considered a request for withdrawal of the application.

We acknowledge receipt of your amendments dated March 11, 2013, March 13, 2013, and March 18, 2013. You may cross reference applicable sections of these amendments 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 Regulatory Project Managers, LCDR Jeremy Wally, Ph.D. or Kirk Prutzman, Ph.D., at (301) 796-2640.

Sincerely yours,

Wellington Sun, M.D.
Director
Division of Vaccines and
Related Products Applications
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Research and Review
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