

Statistical Review Addendum, Q-Pan

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Biostatistics and Epidemiology
Division of Biostatistics

BLA/Supplement Number: 125419.0.37

Product Name: Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted

Indication(s): Active immunization for the prevention of disease in persons 18 years of age and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine

Applicant: ID Biomedical Corporation of Quebec / GSK Biologicals

Date of Submission: May 24, 2013

Action Due Date: November 23, 2013

Review Priority: Standard, resubmission

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1. EXECUTIVE SUMMARY

BLA 125419 was submitted on Feb 22, 2012, by GSK for the AS03 adjuvanted Influenza A (H5N1) Virus Monovalent Vaccine manufactured in Quebec (also referred to as Q-Pan H5N1), indicated for the prevention of disease in persons 18 years of age and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine. On Mar 22, 2013, CBER issued a CR letter requesting additional study FLU Q-PAN-002 D364 datasets, comparisons between the D182 and D364 datasets, and revision of the D42 and D182 unsolicited AE summary tables based on the final D364 data. GSK submitted the complete response to the CR letter in Amendment 37 on May 24, 2013.

This review focuses on the updated AE summary results submitted in Amendment 37 and serves as an addendum to the statistical review of the original submission.

The applicant's updated Day 42 and Day 182 safety analysis results generated using the final Day 364 dataset showed that none of the differences identified have an impact on the safety conclusions presented in previous reports. The applicant has provided adequate responses to the CR comments. Therefore, I recommend approval of Q-Pan H5N1. .

2. BACKGROUND

GSK filed BLA 125419 on Feb 22, 2012, to seek licensure for their AS03 adjuvanted Influenza A (H5N1) Virus Monovalent Vaccine manufactured in Quebec (also referred to as Q-Pan H5N1). On Mar 22, 2013, CBER issued a CR letter which contained items regarding the safety data of the pivotal study FLU Q-PAN-002. The information requested included additional D364 datasets, comparisons between the D182 and D364 datasets, and revision of the D42 and D182 unsolicited AE summary tables based on the final D364 data.

The additional safety datasets and the datasets for side-by-side comparisons between the D182 and D364 data were submitted in Amendments 34 – 36. On May 24, 2013, GSK submitted the last part of the complete response to the CR letter to Amendment 37, providing the updated information on the D42 and D182 AE summary results based on the final D364 data.

During the review of STN 125419.0.37, another GSK sBLA application (STN 125163.253), which used the final study report of the efficacy study FLU Q-QIV-006 to support traditional approval of *FluLaval* (manufactured using the same process as used to make Q-Pan H5N1), was approved on Aug 15, 2013. In a meeting on February 14, 2011 under IND 13413, CBER had informed GSK that this study FLU Q-QIV-006 could serve as the required study to fulfill the Accelerated Approval Regulations for approval of Q-Pan H5N1. Therefore, since this study has already been completed and supported the approval of *FluLaval*, the approval pathway for Q-Pan H5N1 was changed to traditional approval.

This review is an addendum to the original review which was completed before the CR letter was issued. The review will focus on the updated AE summary results submitted in Amendment 37.

3. STATISTICAL EVALUATION

Study FLU Q-Pan-002, 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,” was originally designed to have the subjects followed for safety for 182 days after immunization, with two safety summary reports generated at D42 and D182. The safety follow-up was later extended to D364 at CBER’s request due to the safety concern for the novel adjuvant used. Additions and corrections to safety data collected at earlier time points were registered to the database by study investigators throughout this extended follow-up interval. As a result, if the D364 database is used to generate the D42 and D182 safety reports, there are some differences relative to the D42 and D182 results presented in the original BLA submission.

Results of D42 and D182 safety analyses based on D364 dataset, Study Q-Pan-002

Most of the AE summary tables in the text of the original report and supplements were changed due to changes to the data (corrections, additions, deletions), adjustments in AE coding, and adjustments in formatting. Specifically, changes were noted for Tables 6, 36, 37, 38, 40, 41, 42, 43, 45, 46, 48, 49, and 50, and Supplements 51, 53, 54, 137, 139, 145, 161, 163, 168, 185, 187, and 191. All differences identified are very small in magnitude, and do not have impact on the safety conclusions presented in the previous D42 and D182 study reports.

4. CONCLUSIONS

The applicant's updated Day 42 and Day 182 safety analysis results generated using the final Day 364 dataset showed that none of the differences identified have an impact on the safety conclusions presented in previous reports. The applicant has provided adequate responses to the CR comments. I recommend approval.