

Conference Call, November 29 2012-Q-Pan

Date and Time:

November 28, 2012, 8:30 AM - 10:00 AM

Location:

CBER Conf. WOC2-2201; Conference call

STN #:

125419/0

Sponsor:

ID Biomedical Corporation of Quebec (dba GlaxoSmithKline Biologicals)

Product:

Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted

CBER/FDA Attendees

Anissa Cheung
Carmen Collazo-Custodio
Hana Golding
Manju Joshi
Surender Khurana
Tsai-Lien Lin
William McCormick
Kirk Prutzman
Jeremy Wally
Jerry Weir

GSK Attendees

Dominique Barbeau
Robert Brobst
Sandra Gilbert
David Le Tallec
Marie-Christine Marchland
Pierre-Alain Moisset
Michael Schwartz

1.0

PURPOSE

The objective of this conference call was:

- To discuss GSK's SRID potency specifications for Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted.

2.0

BACKGROUND

On November 27, 2012, GSK provided a slide presentation in which they discuss their proposal for the SRID specifications for the ---(b)(4)----- final container (see Attachment 1). This conference call was held on November 28, 2012 (see item 3.0 Discussion Topics) as a follow-up to a previous discussion we had with GSK on August 16, 2012. During the conference call held on August 16, 2012, CBER noted that GSK did not conduct the SRID testing potency calculations using the standard SRID method based on CBER's guidelines. GSK briefly described their analysis and statistical calculations based on the WHO Guidelines on Stability Evaluation of Vaccines.

3.0

DISCUSSION TOPICS

GSK's Presentation

- GSK presented the slides provided on November 27, 2012, which included an overview of the history of the BLA submission and the advice given during the IND phase of the candidate vaccine. GSK's proposed criteria for HA potency specifications are below (also shown on slide 12 titled "Historical Requirements Applied to Pandemic Candidate Vaccine"):

	Mean Result (µgHA/mL)	Assay Variability	Assay Replicates
---(b)(4)----- Release	(b)(4)	---(b)(4)-----	(b)(4)
Final Container Release and End of Shelf Life	(b)(4)	---(b)(4)-----	Min 3-gel

Open Discussion (once the slide presentation concluded, the following items were discussed):

- CBER asked what is meant by "at least 3 valid gels are required to calculate the mean" (slide 15 titled "Proposed FC Requirements for Pandemic Vaccine"). GSK responded that they routinely run -(b)(4)- for the final container and all gels that meet the assay validity criteria are used for the calculation of HA content. They use a minimum of 3 valid gels to calculate the mean. "Valid" gels are gels that meet the *acceptance criteria* for the SRID assay and these acceptance criteria are the same as those applied for the seasonal vaccine. The -(b)(4)- are performed to avoid the need for repetition of the assay, especially important during a pandemic situation. Variation greater than ----- --(b)(4)-- in the gels performed leads to rejection of assay results.

- CBER noted that the Minimum Release Acceptance Criteria are different for the --- (b)(4)----- Final Container (FC) (slide 12).GSK responded that the overage is built in to sustain the shelf life.They are tightening the assay variability (there is more precision incorporated in the release model), and whereas the -----(b)(4)-----, the FC calculations include all valid assay replicates (- (b)(4)-- are run routinely and the test results will include all valid gels, with a minimum of 3 gels required).One value is reported globally for FC release and stability.
- GSK noted that the expiry acceptance criterion was revised in September 2012 and submitted to the BLA.Any reportable mean result below (b)(4) mg HA/mL is considered “Out of Specification (OOS)” (slide 15).CBER explained that the intent of the historical specifications applied to seasonal influenza virus vaccines is that 15 mg HA/mL is the mean result and (b)(4) mg HA/mL is the lower confidence.GSK responded that if these criteria are applied, one clinical lot (lot AFLIPA109A) would be “OOS” at release (slide 17 titled “Overview of Manufactured Lots and Impact of 95% LCB at (b)(4) mg HA/mL”). This lot was used in clinical study Q-PAN H5N1-002 and the clinical data was used to support the BLA submission. Furthermore, the shelf-life of the vaccine would be significantly reduced (predicted 12 months).Overall, the impact of applying a 95% LCB at (b)(4) µg HA/mL could lead to a 10-20 % increase in overage, resulting in a decrease in the HHS stockpile, a decrease in manufacturing capacity, and an increase in manufacturing cost (slide 19 titled “Impacts of 95% LCB at (b)(4) mg HA/mL”).
- Once the discussion concluded, CBER agreed to provide feedback to GSK after having the opportunity of discussing this issue internally.

4.0

CBER’s CONCLUSIONS AND RECOMMENDATIONS

Based on GSK’s presentation and subsequent discussion, it seems that GSK will release their product based on the following proposed criteria: the accepted mean result for ---(b)(4)----- will be **(b)(4)** mg HA/mL and the final container will be targeted at ≥ 15 mg HA/mL with an accepted mean result of **(b)(4)** mg HA/mL. The potency assay variability has to be -----(b)(4)----- for both -----(b)(4)---- and final container. While there are some differences with GSK’s proposal as compared with what CBER typically accepts for seasonal influenza virus vaccines (discussed above), CBER agrees with GSK’s proposal noting that this is thought of as being a unique situation for the Q-Pan H5N1 influenza virus pandemic vaccine (which is dose sparing and contains an adjuvant) as compared to seasonal influenza virus vaccines.The proposed criteria are being considered without impact to CBER’s long history for handling unadjuvanted inactivated seasonal influenza virus vaccines lot release.

**ATTACHMENT 1: GSK’s Presentation entitled
“Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted Potency
Specifications
for US Licensure”**