

# Meeting Minutes, March 11, 2013-Q-Pan

## MEETING SUMMARY

### Date and Time:

March 11, 2013 12:30 pm – 1:30 pm

### Location:

WOC2 – Room 2330

### STN #:

125419/0

### Sponsor:

ID Biomedical Corporation of Quebec (dba GlaxoSmithKline Biologicals)

### Product:

Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted

### CBER/FDA Invitees

<b>Attended Committee Member</b>	<b>Review Assignment</b>	<b>Supervisor</b>
Carmen Collazo-Custodio	Chair	Elizabeth Sutkowski
Jeremy Wally	Lead RPM	Elizabeth Sutkowski
Kirk Prutzman	Co-RPM	Elizabeth Sutkowski
Andrea James	Clinical	Lewis Schrager
Hana Golding	Product CMC	Jerry Weir
Surender Khurana	Product CMC	Hana Golding
Nabil Al-Humadi	Toxicology	David Green
Tsai-Lien Lin	Clinical/Assay Stats	Dale Horne
Tielin Qin	Assays Stats	Dale Horne
Maryann Gallagher	Advertising/Promotional Labeling	Lisa Stockbridge
Cheryl Hulme	Lot Release	Joseph Quander III

<b>Attended Committee Member</b>	<b>Review Assignment</b>	<b>Supervisor</b>
Yandong Qiang	Pharmacovigilance	Wei Hua
Hector Izurieta	Epidemiology (Effectiveness)	Richard Forshee
Anthony Hawkins	BIMO	Patricia Holobaugh
Randa Melhem	Facilities/DMPQ	Chiang Syin
Jei He	Facilities/DMPQ	Chiang Syin
James Kenney	Product Quality	Rajesh Gupta
Manju Joshi	Product Quality	William McCormick
Lokesh Bhattacharyya	Product Quality	William McCormick
Karen Campbell	Product Quality	William McCormick
David Schwab	Electronic Integrity	Review Laraine Henchal

#### **OTHER ATTENDEES:**

Elizabeth Sutkowski  
Wellington Sun  
Anissa Cheung  
Erik Henchal  
Richard Forshee  
Jerry Weir

### **1.0 PURPOSE**

The objectives of this meeting were:

- A. To update Management on the review progress
- B. To update the review team on the new review timelines including plans to issue a CR letter
- C. To discuss remaining topics that need to be addressed before the Action Due Date

### **2.0 BACKGROUND**

The proposed indication and usage of BLA STN 125419:

Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted is indicated for active immunization against disease caused by the influenza A virus H5N1 subtype contained in the vaccine. Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted is approved for use in persons 18 years of age and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.

### **3.0 DISCUSSION TOPICS**

#### **3.1 Milestones and Meetings**

## **Milestones**

<b>Milestones</b>	<b>Projected Date</b>
Application Received	February 22, 2012
Committee Assignment	March 7, 2012 (FDA Tracked Milestone)
1st Committee Meeting	March 12, 2012
Filing Meeting	April 9, 2012
Filing Letter Issued	April 22, 2012
1st draft reviews	June 21, 2012
Mid-Cycle Review Meeting	July 20, 2012 (FDA Tracked Milestone)
2nd draft reviews	August 30, 2012
Final Reviews (Signed/Uploaded)	October 14, 2012 (Delayed by Major Amend.)
Present to PeRC	September 26, 2012
Labeling Comments to Sponsor	November 9, 2012 (FDA Tracked Milestone)
First Action Due	December 22, 2012
Final Reviews (Signed/Uploaded)	February 4, 2013 (Updated due date)
Notify GSK of PMC/PMR	February 15, 2013
Labeling Complete	March 5, 2013
<b>Major Amendment Action Due Date</b>	<b>March 23, 2013</b>

## **Meetings**

First Committee Meeting:

March 6, 2012

Filing Meeting:

April 9, 2012

Monthly Team Meetings:

May 8, 2012

June 11, 2012

July 9, 2012

August 3, 2012 (revised date)

August 31, 2012 (revised date – Sept. Meeting)

October 5, 2012 (revised date)

**November 6, 2012 (revised date)**

December 10, 2012

January 7, 2013

February 11, 2013

**March 11, 2013**

**Mid-Cycle Review Meeting:**

## **July 20, 2012**

PeRC:

September 26, 2012

VRBPAC:

November 14

SWG:

## **Not Scheduled**

Labeling Meetings:

October 22, 2012

October 25, 2012

November 2, 2012

December 14, 2012

December 20, 2012

January 7, 2013

February 5, 2013

February 8, 2013

### 3.2 Team Reports:

#### 3.2.1 Chair

The chair informed that team that a CR letter will be issued for this BLA and is in the process of being drafted. The chair asked the review team members if there are any additional items that need to be included in this CR letter (other than those described below) and no other items were identified. The chair noted that currently the only outstanding Information Requests relate to our comments on the package insert. Finally, the chair stated that the language for the proposed agreements, PMRs and one PMC is still being finalized.

#### 3.2.2 Clinical

The clinical reviewer stated that issues with the datasets submitted to the BLA for the pivotal study were recently identified during labeling negotiations, and after discussion with GSK on March 8, 2013, it was agreed that the final datasets need to be submitted along with additional relevant information. It was necessary to issue a CR Letter because a thorough review of the updated, final datasets could not be completed by the March 23, 2013 action due date. The clinical reviewer discussed that the details of how this additional information will be submitted to the BLA are still being worked out with GSK. The clinical reviewer further noted that labeling negotiations are still ongoing and may potentially be impacted by the new information that will be submitted in response to

the CR letter. Finally, the clinical reviewer indicated that a revised *Request for Deferral of Pediatric Studies* was recently submitted to the BLA. GSK revised the timeline for the proposed pediatric clinical studies. This revision is adequate.

### 3.2.3 Statistical

The statistical reviewer noted that finalization of the clinical statistical review will not be possible until GSK submits the information described above.

### 3.2.4 CMC/Product

The CMC reviewer noted that GSK has submitted reports for stability studies in response to the extractable/leachable Information Request sent to GSK on February 20, 2013, and that the reviewer is satisfied with the results of these studies. No further comments on this issue are forthcoming.

### 3.2.5 Facilities/DMPQ

Review Uploaded to EDR

### 3.2.6 Pharmacovigilance

The Pharmacovigilance reviewer noted that the details of a potential PMC (pregnancy Registry) and a request for expedited reporting time frame of AIH and Narcolepsy are still being discussed by OBE management and that they should be providing final language to the review team in a few days.

### 3.2.7 DBSQC and Lot Release

Review Uploaded to EDR

### 3.2.8 Toxicology

Review Uploaded to EDR

### 3.2.9 Epidemiology (Effectiveness Study)

Review Uploaded to EDR

### 3.2.10 BIMO

Review Uploaded to EDR

### 3.2.11 APLB

Review Uploaded to EDR

## 4.0 Information Requests / Amendments

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
4/30/2012a	Carmen Collazo-	IR for Pediatric Plan, stability	Andrea James, Hana	125419/0.3 125419/0.4	Yes	Surender Khurana –

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
	Custodio	data, clinical assay validation, HA content by SRID validation, other assay validation, facilities information, pharmacovigilance	Golding, Surender Khurana, Tsai-Lien Lin, Tielin Qin, Manju Joshi Lokesh Bhattacharyya, <b>Yandong Qiang</b> , Randa Melhem	<b>125419/0.5</b> 125419/0.11		125419/0.4 Hana Golding – 125419/0.4 Lokesh Bhattacharyya – 125419/0.4, 125419/0.11 Manju Joshi – 125419/0.4 Randa Melhem – 125419/0.3, 125419/0.4 <b>Collazo – 125419/0.1 (memo pending)</b> Manju Joshi – 125419/0.2 (test results)
4/30/2012b	Carmen Collazo-Custodio	Revised 356h form, SRID testing reagents and results	<b>Carmen Collazo</b> , Karen Campbell	<b>125419/0.1</b> 125419/0.2	<b>Yes</b>	
6/15/2012	Carmen Collazo-Custodio	Questions about location of information in the submission.	---	---	No	
6/21/2012	Carmen Collazo-Custodio	Adjuvant lots and SRID calculation spreadsheet	Karen Campbell	---	No	
7/30/2012	Carmen Collazo-Custodio	Product Manufacturing Questions	James Kenney, Hyesuk Kong, Karen Campbell, Surender Khurana, Randa Melhem	125419/0.6 125419/0.9 125419/0.10	No	Surender Khurana – 125419/0.9, 125419/0.10 Karen Campbell – 125419/0.6 (LRP) James Kenney – 125419/0.9 (11/16/2012 Memo) Manju Joshi – 125419/0.10

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
8/10/2012	Kirk Prutzman	AS03 Manufacturing Quality	Randa Melhem	125419/0.8	No	Hana Golding – 125419/0.8 Randa Melhem – 125419/0.8
8/15/2012	Kirk Prutzman	Follow questions to GSK's responses to questions 16, 17d, 18, 21, 22 from the 4/30/2012 IR	Lokesh Bhattacharyya	125419/0.11	No	Lokesh Bhattacharyya – 125419/0.11
8/16/2012	Carmen Collazo-Custodio	IR Regarding GSK's SRID Results	Manju Joshi, Rajesh Gupta, Karen Campbell	125419/0.7 125419/0.10	No	Manju Joshi – 125419/0.7, 125419/0.10 (12/6/2013 memo)
9/10/2012	Jeremy Wally	Response on Timing of Amendment Submission	---	---	No	
9/25/2012	Jeremy Wally	IR regarding SRID assay and additional comments on VRBPAC and Proper Name	Manju Joshi Carmen Collazo-Custodio	125419/0.10	No	Manju Joshi – 125419/0.10 (12/6/2013 memo)

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
9/26/2012	Jeremy Wally	September 25, 2012, IR/Comments Follow-Up Comments regarding the	---	---	No	
9/28/2012	Carmen Collazo-Custodio	Pharmacovigilance Plan for Influenza A (H5N1) Virus Monovalent Vaccine (Version	Yandong Qiang	125419/0.17	Yes	



Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
		----(b)(4)----- ----- )				Randa Melhem – 125419/0.18
Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
11/9/2012	Kirk Prutzman	<i>PI, Carton, Container comments to GSK</i>		125419/0.20 125419/0.21	<b>Yes</b>	Hana Golding – 125419/0.20, 125419/0.21 <b>Labeling Memo Pending</b>
11/9/2012	Kirk Prutzman	IR regarding HA minimum release acceptance criterion	Tsai-Lien Lin Hana Golding Surender Khurana Manju Joshi	125419/0.20	No	Hana Golding – 125419/0.20
11/16/2012	Carmen Collazo-Custodio	<i>Additional comments on the Package Insert and the Carton Labels</i>		125419/0.21	<b>Yes</b>	Hana Golding – 125419/0.21 <b>Labeling Memo Pending</b>
11/19/2012	Kirk Prutzman	IR Regarding Lot Release Protocol in Amendment 13	Catherine Poole	125419/0.19	No	Karen Campbell – 125419/0.19 (LRP)
11/20/2012	Kirk Prutzman	Additional IR item regarding Lot Release Protocol	Catherine Poole	125419/0.19	No	Karen Campbell – 125419/0.19 (LRP)
11/20/2012	Kirk Prutzman	IR regarding Amendment 16 submitted on November 15, 2012	<b>Andrea James</b>	<b>125419/0.19</b>	<b>Yes</b>	

<b>Request Date</b>	<b>CBER Rep(s)</b>	<b>Request</b>	<b>CBER Requester for Info</b>	<b>BLA Amendment Response</b>	<b>Review Pending?</b>	<b>Reviewed by and Date Reviewed</b>
11/26/2012	Carmen Collazo-Custodio	IR Regarding the Ste. Foy and the Rixensart/Wavre facilities	Randa Melhem	125419/0.22	No	Randa Melhem – 125419/0.22
11/28/2012	Carmen Collazo-Custodio	Conference Call Summary and CBER's Response to GSK's Potency Specifications Proposal	---	---	No	
11/29/2012	Carmen Collazo-Custodio	Characterization of new working seed banks	<b>Surendur Khurana</b>	<b>125419/0.19</b>	<b>Yes</b>	
11/29/2012	Carmen Collazo-Custodio	Clarification on environmental monitoring qualifications studies performed at the Rixensart facility	Randa Melhem	125419/0.22	No	Randa Melhem – 125419/0.22
11/30/2012	Carmen Collazo-Custodio	IR regarding cleaning validation	Randa Melhem	125419/0.22	No	Randa Melhem – 125419/0.22

<b>Request Date</b>	<b>CBER Rep(s)</b>	<b>Request</b>	<b>CBER Requester for Info</b>	<b>BLA Amendment Response</b>	<b>Review Pending?</b>	<b>Reviewed by and Date Reviewed</b>
11/30/2012	Carmen Collazo-Custodio	Follow-up discussion regarding the telephone conversation held on November 29, 2012, in which CBER requested clarification on discrepancies found on environmental monitoring qualifications	Randa Melhem	125419/0.22	No	Randa Melhem – 125419/0.22

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
11/30/2012	Carmen Collazo-Custodio	studies performed at the Rixensart facility. Information request regarding the description of a reproductive and developmental toxicity study described in the PI.	<b>Andrea James</b> Nabil Al-Humadi	<b>125419/0.21</b>	<b>Yes</b>	Nabil Al-Humadi – 125419/0.21
12/3/2012	Carmen Collazo-Custodio	Request to clarify if ----- ------(b)(4)----- -----.	Randa Melhem	125419/0.22	No	Randa Melhem – 125419/0.22
12/5/2012	Carmen Collazo-Custodio	Conference call with GSK to discuss documents/reports translated from French containing inconsistent information. CBER's comments to GSK's response submitted on November 30, 2012, regarding the proposed Lot Release Protocol.	Randa Melhem	125419/0.22	No	Randa Melhem – 125419/0.22
12/5/2012	Carmen Collazo-Custodio	IR Regarding Cleaning Validation information	Karen Campbell	125419/0.23	No	Karen Campbell – 125419/0.23
12/19/2012	Kirk Prutzman	IR on alternative -- ------(b)(4)----- used to storage the H5N1 ----- (b)(4)-----	Randa Melhem	125419/0.23	No	Randa Melhem – 125419/0.23
12/20/2012	Carmen Collazo-Custodio	IR Regarding Cleaning Validation information	Randa Melhem Surender Khurana	125419/0.26	No	Randa Melhem – 125419/0.26
12/21/2012	Carmen	<i>Second Round or</i>		<b>125419/0.24</b>	<b>Yes</b>	<b>Labeling</b>

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
1/22/2013	Collazo-Custodio Kirk Prutzman	<i>Carton/Container comments</i> IR Regarding LRP	Karen Campbell	125419/0.23	No	<b>Memo Pending</b> Karen Campbell – 125419/0.23

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
1/14/2013	Jeremy Wally	<i>Second Round of PI Labeling</i>		125419/0.25	Yes	<b>Labeling Memo Pending</b>
1/22/2013	Jeremy Wally	Tcon with GSK: IR regarding shipping validations and shipping protocols	Randa Melhem	125419/0.26	No	Randa Melhem – 125419/0.26
2/6/2013	Jeremy Wally	Discussion of Narcolepsy Extractables and Leachables studies for the ----	---	---	No	
2/8/2013	Carmen Collazo-Custodio	(b)(4)--- are limited and the data are insufficient to draw any conclusions about the appropriateness of these (b)(4) for ---	Randa Melhem Surender Khurana	125419/0.27	No	Randa Melhem – 125419/0.27
2/11/2013	Carmen Collazo-Custodio	(b)(4)--- storage. GSK response to CBER comments of Feb. 8, 2013 – GSK decided to remove the information submitted in the BLA regarding the use of -----(b)(4)----- for storage of the ---(b)(4)----- in response to	---	---	No	

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
2/12/2013	Carmen Collazo-Custodio	<p>CBER's comments provided on February 8, 2013.</p> <p><i>Third round of review on container and carton labels.</i></p>		125419/0.28	Yes	Labeling Memo Pending
2/12/2013	Carmen Collazo-Custodio	<p>GSK-request for clarification carton/container comments – GSK conducted an initial review of CBER comments on the container/carton labels provided on February 12, 2013, and have a question regarding consistency of the use of the word vial(s).</p> <p>Additional</p>	---	---	No	
2/14/2013	Carmen Collazo-Custodio	<p>comments on third round of review on container and carton labels.</p>		125419/0.28	Yes	Labeling Memo Pending
Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
2/20/2013	Carmen Collazo-Custodio	<p>Comments regarding leachables studies</p>	Surender Khurana	125419/0.29	Yes	
2/20/2013	Carmen Collazo-Custodio	<p>Exemptions from General Safety Testing - CBER's feedback on GSK's request for exemptions from</p>	---	---	No	

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending?	Reviewed by and Date Reviewed
		General Safety Test for both AS03 adjuvant and Quebec H5N1 antigen				
2/25/2013	Kirk Prutzman	Communication of UNII Code assignments	---	---	No	
3/1/2013	Kirk Prutzman	<i>Third Round of PI Labeling</i>			Yes	<b>Labeling Memo Pending</b>

## 5.0 Amendments

Date/STN	Summary
May 3, 2012 (125419/0.1)	Partial response to 4/30/2012b IR. Revised 356h form.
May 25, 2012 (125419/0.2)	Partial response to 4/30/2012b IR. Answers to Item 2.
June 20, 2012 (125419/0.3)	Partial response to 4/30/2012a IR. Answers to Items 24-34 (facilities).
July 18, 2012 (125419/0.4)	Partial response to 4/30/2012a IR. Answers to Items 2-23 and 35-36.
July 19, 2012 (125419/0.5)	Partial response to 4/30/2012a IR. Answer to Item 1. All responses to IR now submitted.
August 13, 2012 (125419/0.6)	Partial response to 7/30/2012 IR. Answer to Item 1. Addition of Robert D. Brobst as secondary POC
August 29, 2012 (125419/0.7)	Response to 8/16/2012 tcon; updated 356h form; updated list of POC's.
September 10, 2012 (125419/0.8)	Response to 8/10/2012 tcon
September 14, 2012 (125419/0.9)	Response to Questions 2, 3, and 5-18 from CBER's 7/30/2012 IR.
September 28, 2012	Response to Information Requests dated July 30, 2012, August 16, 2012, and September 25, 2012.

<b>Date/STN</b>	<b>Summary</b>
(125419/0.10) October 10, 2012	Response to Information Requests dated April 30, 2012, and August 15, 2012.
(125419/0.11) October 18, 2012	Response to IR from CBER dated October 2, 2012
(125419/0.12) October 26, 2012	Response to IR from CBER dated October 16, 2012 regarding the LRP
(125419/0.13) November 5, 2012	Response to IR from CBER dated October 18, 2012 regarding the Anti-Microbial Effectiveness Testing
(125419/0.14) November 6, 2012	Response to 2 IRs from CBER dated October 15, 2012, and October 31, 2012, regarding clinical issues
(125419/0.15) November 15, 2012	Response to IR from CBER dated October 17, 2012, regarding subgroup analyses of all primary immunogenicity and safety endpoints by age, race and gender in studies Qpan-001, Q-Pan-002 and the ISS analyses.
(125419/0.16) November 19, 2012	Responses to 3 Information Requests from CBER dated 9/28/2012, 10/10/2012, and 10/22/2012 regarding the PVP.
(125419/0.17) November 30, 2012	Responses to 2 Information Requests from CBER dated 10/17/2012, and 11/8/2012.
(125419/0.18) November 30, 2012	Responses to 5 Information Requests from CBER dated 11/5/2012, and 11/19/2012, 2 lrs on 11/20/2012, and 11/29/2012.
(125419/0.19) December 4, 2012	Response to PI labeling comments from CBER on November 9, 2012. Response to MRAC IR from CBER dated November 9, 2012.
(125419/0.20) December 8, 2012	Response to Carton and Container comments from CBER on November 9, 2012 and November 16, 2012. Response to comments regarding the toxicity study described in Section 8.1, Pregnancy, of the proposed Package Insert from CBER date November 30, 2012.
(125419/0.21) December 13, 2012	Response to information requests from CBER dated 11/26/2012, 11/30/2012, and 12/3/2012. Response to questions from telephone-tcons dated 11/29/2012, 11/30/2012, and 12/5/2012.
(125419/0.22) January 21, 2013	Response to information requests from CBER dated 12/5/2012, 12/19/2012, and 1/2/2013.
(125419/0.23)	

<b>Date/STN</b>	<b>Summary</b>
January 24, 2013 (125419/0.24)	Response to Carton and Container comments from CBER on December 21, 2012.
February 1, 2013 (125419/0.25)	Response to 1/14/2013 Second round of PI labeling comments. Additional rationale for PI Sections 6.1 and 5.2 are included.
February 1, 2013 (125419/0.26)	Response to information requests from CBER dated 12/20/2012 and 1/22/2013.
February 18, 2013 (125419/0.27)	Response to information requests from CBER dated 2/8/2013.
February 22, 2013 (125419/0.28)	Response to Carton and Container comments from CBER on February 12, 2013. <b>FINAL/ACCEPTABLE VERIONS OF CARTON AND CONTAINER LABELS</b>
February 27, 2013 (125419/0.29)	Response to information request from CBER dated 2/20/2013.
March 1, 2013 (125419/0.30)	Response to information request from CBER dated 2/6/2013. New Pediatric Plan