

**MEETING SUMMARY**

Date and Time:	February 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

Attended	Committee Member	Review Assignment	Supervisor
✓	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
✓	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 Henschel

OTHER ATTENDEES:

Anissa Cheung	Wellington Sun
Richard Forshee	Elizabeth Sutkowski
Marion Gruber	
Erik Henschel	
Lewis Schrager	

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
- 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

Milestone	Projected Date
▪ 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
▪ Major Amendment Action Due Date	March 23, 2013

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:

PeRC:

VRBPAC:

SWG:

Labeling Meetings:

July 20, 2012

September 26, 2012

November 14

Not Scheduled

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

Management and reviewers were reminded of the new due dates (above). Reviewers were asked to report any PMCs they proposed to be included in the Approval Letter.

3.2.2 Clinical

Clinical provided an update on a conference call with GSK held on February 6, 2013. During the call, CBER asked if GSK has considered modifying the planned pediatric protocols to exclude subjects expressing the DQB1*0602 HLA allele associated with narcolepsy. GSK agreed to evaluate having this exclusion in the planned protocols and to provide feedback to CBER on this issue within 2 weeks.

Clinical also indicated that the reviewer is considering the inclusion of narcolepsy in the “Warnings and Precautions” section and/or the “Post-marketing Experience” section of the Prescribing Information currently under review.

3.2.3 Statistical

Reviews have been completed.

3.2.4 CMC/Product

The Division of Viral Products is not recommending any PMCs. Data accrued from ongoing stability studies will be provided in Annual Reports.

3.2.5 Facilities/DMPQ

Reviewer is finalizing the review memo.

3.2.6 Pharmacovigilance

Reviewer is considering recommending the establishment of a pregnancy registry in the U.S. and 15-day expedited reports of AIH and Narcolepsy.

3.2.7 DBSQC and Lot Release

Reviews 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 PLB

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-Custodio	IR for Pediatric Plan, stability data, clinical assay validation, HA content by SRID validation, other assay validation, facilities information, pharmacovigilance	Andrea James, Hana Golding, Surender Khurana, Tsai-Lien Lin, Tielin Qin, Manju Joshi Lokesh Bhattacharyya, Yandong Qiang, Randa Melhem	125419.3 125419.4 125419.5 125419.11	Yes	Surender Khurana – 125419.4 Hana Golding – 125419.4
4/30/2012b	Carmen Collazo-Custodio	Revised 356h form, SRID testing reagents and results	Carmen Collazo, Karen Campbell	125419.1 125419.2	Yes	
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	125419.6 125419.9 125419.10	Yes	Surender Khurana – 125419.9 125419.10
8/10/2012	Kirk Prutzman	AS03 Manufacturing Quality	Randa Melhem	125419.8	Yes	

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending ?	Reviewed by and Date Reviewed
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	125419.11	Yes	
8/16/2012	Carmen Collazo-Custodio	IR Regarding GSK's SRID Results	Manju Joshi, Rajesh Gupta, Karen Campbell	125419.7 125419.10	Yes	
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	125419.10	Yes	
9/26/2012	Jeremy Wally	September 25, 2012, IR/Comments Follow-Up	-	-	No	
9/28/2012	Carmen Collazo-Custodio	Comments regarding the Pharmacovigilance Plan for Influenza A (H5N1) Virus Monovalent Vaccine (Version 2: July 2012*) provided in the submission of July 18, 2012.	Yandong Qiang	125419.17	Yes	
10/2/2012	Kirk Prutzman	IR for qualification test reports for the AS03 Adjuvant	James Kenney	125419.12	Yes	
10/10/2012	Carmen Collazo-Custodio	IR regarding the PVP	Yandong Qiang	125419.17	Yes	
10/15/2012	Kirk Prutzman	IR Regarding Clinical Items	Andrea James	125419.15	Yes	
10/16/2012	Carmen Collazo-Custodio	IR Regarding Lot Release Protocol	Karen Campbell	125419.13	Yes	
10/17/2012	Carmen Collazo-Custodio	IR comments: clinical (subgroup analyses) and clarification on filling of AS03 (----- ----(b)(4)-----)	Andrea James Tsai-Lien Lin Randa Melhem	125419.16 125419.18	Yes	
10/18/2012	Kirk Prutzman	IR Regarding Anti-Microbial Effectiveness Testing	James Kenney	125419.14	Yes	
10/22/2012	Carmen Collazo-Custodio	IR comment on GSK's PVP	Yangdong Qiang	125419.17	Yes	
10/31/2012	Carmen Collazo-Custodio	Request for CRFs for subjects in study Q-Pan-002	Andrea James	125419.15	Yes	
11/5/2012	Kirk Prutzman	IR regarding---(b)(4)----- levels in the Adjuvant	Hana Golding	125419.19	Yes	
11/8/2012	Carmen Collazo-Custodio	IR regarding further clarification on filling of AS03 (----- ----(b)(4)-----)	Randa Melham	125419.18	?	
11/9/2012	Kirk Prutzman	<i>PI, Carton, Container comments to GSK</i>		125419.20 125419.21		
11/9/2012	Kirk Prutzman	IR regarding HA minimum release acceptance criterion	Tsai-Lien Lin Hana Golding Surender Khurana Manju Joshi	125419.20	Yes	
11/16/2012	Carmen Collazo-Custodio	<i>Additional comments on the Package Insert and the Carton Labels</i>		125419.21		

Request Date	CBER Rep(s)	Request	CBER Requester for Info	BLA Amendment Response	Review Pending ?	Reviewed by and Date Reviewed
11/19/2012	Kirk Prutzman	IR Regarding Lot Release Protocol in Amendment 13	Catherine Poole	125419.19	Yes	
11/20/2012	Kirk Prutzman	Additional IR item regarding Lot Release Protocol	Catherine Poole	125419.19	Yes	
11/20/2012	Kirk Prutzman	IR regarding Amendment 16 submitted on November 15, 2012	Andrea James	125419.19	Yes	
11/26/2012	Carmen Collazo-Custodio	IR Regarding the Ste. Foy and the Rixensart/Wavre facilities	Randa Melhem	125419.22	Yes	
11/29/2012	Carmen Collazo-Custodio	Characterization of new working seed banks	Surendur Khurana	125419.19	Yes	
11/30/2012	Carmen Collazo-Custodio	IR regarding cleaning validation	Randa Melhem	125419.22	Yes	
11/30/2012	Carmen Collazo-Custodio	Information request regarding the description of a reproductive and developmental toxicity study described in the PI.	Andrea James Nabil Al-Humadi	125419.21	Yes	
12/1/2012	Carmen Collazo-Custodio	Conference Call Summary and CBER's Response to GSK's Potency Specifications Proposal	---	---	No	
12/3/2012	Carmen Collazo-Custodio	Request to clarify if ----- ----- (b)(4) ----- -----.	Randa Melhem	125419.22	Yes	
12/5/2012	Carmen Collazo-Custodio	CBER's comments to GSK's response submitted on November 30, 2012, regarding the proposed Lot Release Protocol.	Karen Campbell	125419.23		
12/19/2012	Kirk Prutzman	IR Regarding Cleaning Validation information	Randa Melhem	125419.23	Yes	
12/20/2012	Carmen Collazo-Custodio	IR on alternative --- (b)(4) ---- used to storage the H5N1 ----- ---- (b)(4) --	Randa Melhem Surender Khurana	125419.26	Yes	
12/21/2012	Carmen Collazo-Custodio	Second Round or Carton/Container comments		125419.24		
1/2/2013	Kirk Prutzman	IR Regarding LRP	Karen Campbell	125419.23	Yes	
1/14/2013	Jeremy Wally	Second Round of PI Labeling		125419.25	Yes	
1/22/2013	Jeremy Wally	Tcon with GSK: IR regarding shipping validations and shipping protocols	Randa Melhem	125419.26	Yes	

Amendments

Date/STN	Summary
May 3, 2012 (125419.1)	Partial response to 4/30/2012b IR. Revised 356h form.
May 25, 2012 (125419.2)	Partial response to 4/30/2012b IR. Answers to Item 2.
June 20, 2012 (125419.3)	Partial response to 4/30/2012a IR. Answers to Items 24-34 (facilities).

Date/STN	Summary
July 18, 2012 (125419.4)	Partial response to 4/30/2012a IR. Answers to Items 2-23 and 35-36.
July 19, 2012 (125419.5)	Partial response to 4/30/2012a IR. Answer to Item 1. All responses to IR now submitted.
August 13, 2012 (125419.6)	Partial response to 7/30/2012 IR. Answer to Item 1. Addition of Robert D. Brobst as secondary POC
August 29, 2012 (125419.7)	Response to 8/16/2012 tcon; updated 356h form; updated list of POC's.
September 10, 2012 (125419.8)	Response to 8/10/2012 tcon
September 14, 2012 (125419.9)	Response to Questions 2, 3, and 5-18 from CBER's 7/30/2012 IR.
September 28, 2012 (125419.10)	Response to Information Requests dated July 30, 2012, August 16, 2012, and September 25, 2012.
October 10, 2012 (125419.11)	Response to Information Requests dated April 30, 2012, and August 15, 2012.
October 18, 2012 (125419.12)	Response to IR from CBER dated October 2, 2012
October 26, 2012 (125419.13)	Response to IR from CBER dated October 16, 2012 regarding the LRP
November 5, 2012 (125419.14)	Response to IR from CBER dated October 18, 2012 regarding the Anti-Microbial Effectiveness Testing
November 6, 2012 (125419.15)	Response to 2 IRs from CBER dated October 15, 2012, and October 31, 2012, regarding clinical issues
November 15, 2012 (125419.16)	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.
November 19, 2012 (125419.17)	Responses to 3 Information Requests from CBER dated 9/28/2012, 10/10/2012, and 10/22/2012 regarding the PVP.
November 30, 2012 (125419.18)	Responses to 2 Information Requests from CBER dated 10/17/2012, and 11/8/2012.
November 30, 2012 (125419.19)	Responses to 5 Information Requests from CBER dated 11/5/2012, and 11/19/2012, 2 Irs on 11/20/2012, and 11/29/2012.
December 4, 2012 (125419.20)	Response to PI labeling comments from CBER on November 9, 2012. Response to MRAC IR from CBER dated November 9, 2012.
December 8, 2012 (125419.21)	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.
December 13, 2012 (125419.22)	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 .
January 21, 2013 (125419.23)	Response to information requests from CBER dated 12/5/2012, 12/19/2012, and 1/2/2013.
January 24, 2013 (125419.24)	Response to Carton and Container comments from CBER on December 21, 2012.
February 1, 2013 (125419.25)	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	Response to information requests from CBER dated 12/20/2012 and 1/22/2013.

Date/STN	Summary
(125419.26)	