



MEETING SUMMARY

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|-----------------------|---|
| 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 Schragger |
| ✓ | 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 Henchal |

OTHER ATTENDEES:

Anissa Cheung Wellington Sun
Richard Forshee Elizabeth Sutkowski
Marion Gruber
Erik Henchal
Lewis Schragger

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 | <i>Second Round or Carton/Container comments</i> | | 125419.24 | | |
| 1/2/2013 | Kirk Prutzman | IR Regarding LRP | Karen Campbell | 125419.23 | Yes | |
| 1/14/2013 | Jeremy Wally | <i>Second Round of PI Labeling</i> | | 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) | |