

# Meeting Minutes, October 7, 2009 - Flublok

## MINUTES OF INTERNAL MEETING

**Meeting Date:** October 7, 2009

**Meeting Time:** 11:30 AM –1:30 PM

**Meeting Location:** Woodmont Office Complex, Rm 308S

**File:** BLA 125285

**Product Name:** Flublok

**Sponsor:** Protein Science Corporation (PSC)

### FDA Attendees:

Norman Bayor, Loris McVittie, Philip Krause, Jerry Weir, Douglas Pratt, Lewis Schrager, Amelia Horne, Cynthia Nolletti, Maryna Eichelberger, Matthew Sandbulte, Barbara Krasnicka, Lev Sirota, Tsai-Lien Lin, Katherine Matrakas, Rakesh Pandey, Timothy Fritz

### Purpose of Meeting:

To discuss OVR's and OBE's concerns regarding PSC's hemagglutination inhibition (HAI) assay.

### Discussion:

DVP indicated that, after having reviewed the clinical results of the Fluzone vs Flublok non-inferiority studies PSC03 and PSC06 (as summarized in the Clinical Reviewer's draft VRBPAC briefing document), it did not have large concerns regarding PSC's validation of their HAI assay using baculovirus-derived, recombinant hemagglutinin as the antigen.

OBE summarized PSC's validation information in which PSC proposed the criterion that the antibody titers of -b(4)- of the sera used to compare the HAI assay using egg-derived antigen to PSC's HAI assay using baculovirus expressed antigen should differ by -b(4)--. OBE indicated that results from b(4) sera had been used for the validation. It was noted that the FDA had agreed at the pre-BLA meeting that PSC's HAI assay was acceptable. OBE suggested that a criterion in which the ratios of Geometric Mean Titers (GMTs) are  $\leq 1.5$  might have been preferable. The variability of the GMTs determined by PSC's HAI assay was acknowledged and OBE's concerns regarding this variability had been communicated to PSC in CBER's August 29, 2008 CR letter (comment #16). OBE indicated that PSC's had adequately addressed its concerns in their response to the CR letter.

It was noted that antibody titers of Flublok recipients determined using PSC's HAI assay tended to be slightly higher than those determined using egg-derived antigen and it was decided that OBE should analyze the data to determine whether run-to-run variability of the HAI assay used in studies PSC03 and PSC06 could influence the conclusions derived from these studies. OBE indicated that it could provide this analysis within 10 days.

OVRP summarized the immunogenicity and efficacy data from studies PSC01, PSC04, PSC03 and PSC06 and indicated that, in general, the clinical data supported licensure of Flublok in individuals 18 – 49 years old. OBE noted that its review of the study data showed that the primary study hypotheses had not been met and mentioned its concern that PSC took an inordinate amount of time to provide data requested by OBE for study PSC04. OVRP noted that Bioresearch Monitoring (BIMO) had reviewed 3 of the study sites and found no concerns. OBE indicated that it was satisfied by the BIMO investigations.

It was noted that, although PSC has requested traditional approval for persons 18 years and older in their Complete Response (because of additional clinical endpoint data submitted with the CR), the BLA for Flublok was still on an accelerated approval schedule. The issue of granting traditional approval and in which age groups requires

further discussion. Because Flublok efficacy had not been demonstrated for people > 49 years old, particularly in people  $\geq$

65 years old who are at higher risk, it was suggested that extension of licensure of Flublok to individuals > 49 years old would be a topic which may need to be discussed at the November VRBPAC.

It was noted that the VRBPAC briefing document for a closed VRBPAC session, if needed, would be prepared by Jerry Weir and Norman Baylor.