DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

March 12, 2015

VIA FACSIMILE AND UPS (UNITED PARCEL SERVICE)

Samuel Simons
Regulatory Manager
Protein Sciences Corporation
1000 Research Parkway
Meriden, CT 06450

Re: **Flublok (Influenza Vaccine)**
BLA STN# 125285

Dear Mr. Simons:

The Advertising and Promotional Labeling Branch (APLB) at the U.S. Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) has reviewed the video interview with CEO Dr. Manon Cox, entitled 'Watch us on Lifetime – The Balancing Act,' that is posted on the website www.flublok.com by your company, Protein Sciences Corporation (Protein Sciences). This promotional material is in violation of the Federal Food, Drug, and Cosmetic Act (Act) and implementing regulations because it overstates the efficacy of Flublok (Influenza Vaccine) and omits the risks associated with Flublok. Therefore, this material misbrands Flublok under sections 502(a) and 201(n) of the Act, 21 U.S.C. §352(a) and §321(n), and FDA implementing regulations, *Cf.* 21 CFR 202.1(e)(6)(i) and (e)(7)(viii).

Background

According to the FDA-approved prescribing information (PI), Flublok is a vaccine indicated for active immunization against disease caused by influenza virus subtypes A and type B contained in the vaccine. Flublok is approved for use in persons 18 years of age and older.

The Warnings and Precautions section of the PI includes, but is not limited to, the following risks:

> Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of Flubok.
>
> If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of potential benefits and risks.
>
> Vaccination with Flublok may not protect all vaccine recipients.

The Adverse Reactions section includes, but is not limited to, the following:

> In adults 18 through 49 years of age, the most common (≥10%) injection-site reaction was pain (37%); the most common (≥10%) solicited systemic adverse reactions were headache (15%), fatigue (15%) and muscle pain (11%).
>
> In adults 50 through 64 years of age, the most common (≥10%) injection site reaction was pain (32%); the most common (≥10%) solicited systemic adverse reactions were headache (17%), fatigue (13%), and muscle pain (11%).
>
> In adults 65 years of age and older, the most common (≥10%) injection site reaction was pain (19%); the most common (≥10%) solicited systemic adverse reactions were fatigue (13%) and headache (10%).

Misleading Efficacy Claim

Promotional materials are misleading if they represent or suggest that a product is more effective than has been demonstrated by substantial evidence or substantial clinical experience. Your video, entitled 'Watch us on Lifetime – The Balancing Act,' presents an interview with Dr. Cox in which she states that Protein Sciences *'is able to put three times more protein in there, so it is also a high dose vaccine. More protein means your body will form more antibodies that will help you fight the flu.'* This claim misleadingly implies that the higher antigen content of Flublok translates into greater protection. Currently, there is only one licensed high-dose influenza vaccine, which is indicated for active immunization of persons 65 years of age and older against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FDA is unaware of any adequate and well-controlled clinical trials that substantiate this claim for your product. Furthermore, in our October 20, 2014 letter to Protein Sciences on this issue, we provided advisory comments regarding the misleading implication of this claim. We reiterated our comments in a teleconference with Dr. Manon Cox on November 10, 2014.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials.

Specifically, the video presents multiple efficacy claims for Flublok, such as '*helps you fight the flu,*' but fails to present any important safety information from the PI.

Conclusion and Requested Actions

For the reasons discussed above, your promotional material misbrands Flublok under sections 502(a) and 201(n) of the Act, 21 U.S.C. §352(a) and §321(n), and FDA implementing regulations, *Cf.* 21 CFR 202.1(e)(6)(i) and (e)(7)(viii).

We request that Protein Sciences immediately cease the dissemination of this violative promotional material for Flublok, as well as promotional materials with the same or similar claims and representations. Please submit a written response within ten (10) business days of the

date of this letter, stating whether you intend to comply with this request, listing all violative promotional materials for Flublok and explaining your plan for discontinuing use of such materials. Please direct your response to Lisa Stockbridge, Ph.D., Branch Chief at the Food and Drug Administration, Center for Biologics Evaluation and Research, Office of Compliance and Biologics Quality, Division of Case Management, Advertising and Promotional Labeling Branch, 10903 New Hampshire Ave., WO71-G112, Silver Spring, MD 20993-0002. In all future correspondence regarding this matter, please refer to the BLA/STN number. We remind you that only written communications are considered official responses.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Flublok comply with each applicable requirement of the Act and FDA implementing regulations.

If you choose to revise your promotional materials, APLB is willing to assist you in assuring that your revised materials comply with applicable provisions of the Act by reviewing your revisions before you use them in promotion.

Sincerely,

Robert A. Sausville
Director, Division of Case Management
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research