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

REVIEW MEMORANDUM

Date: May 13, 2009

To: Bernard McWatters, Committee Chair, OVRR, DVRPA, CMC1, HFM-478

Anissa Cheung, Regulatory Project Manager, OVRR/DVP, HFM-445

From: Lisa Stockbridge, Ph.D.
Consumer Safety Officer
OCBQ/DCM/APLB, HFM-602

Through: Ele Ibarra-Pratt, RN, MPH
Branch Chief
OCBQ/DCM/APLB, HFM-602

Through: Robert A. Sausville
Director
OCBQ/DCM, HFM-610

Re: **BLA 125297 Agriflu**
Influenza virus trivalent subunit (A/A/B hemagglutinin and neuraminidase; embryonated hen's eggs) Vaccine, Inactivated
Request for Proprietary Name Review

Executive Summary

APLB recommends that the proposed proprietary name Agriflu [Influenza virus trivalent subunit (A/A/B hemagglutinin and neuraminidase; embryonated hen's eggs) Vaccine, Inactivated] be found Acceptable.

Background

The Advertising and Promotional Labeling Branch (APLB) received a request to review Novartis Vaccines and Diagnostics Inc.'s (Novartis) proposed proprietary name, **Agriflu** [Influenza virus trivalent subunit (A/A/B hemagglutinin and neuraminidase; embryonated hen's eggs) Vaccine, Inactivated], in preparation for the approval of BLA 125297. The application received a Complete Response (CR) letter on April 27, 2009.

A former proposed proprietary name, Agrippal, was submitted to IND -b(4)- on March 22, 2007. This proprietary name was found "Tentatively Acceptable with Concerns" by APLB on February 14, 2008. In an e-mail dated March 31, 2008, OVRR informed Novartis that Agrippal was found "Acceptable with Concerns" and that Novartis "should request another proprietary name review of Agrippal closer to the time of approval since a significant amount of time may pass between now and licensure of the product and to ensure that FDA has not approved a product with a conflicting proprietary name in the interim." The April 27, 2009, CR letter stated that Agrippal was "Tentatively Acceptable" and would be reviewed within 90 days of product approval.

On March 13, 2009, Novartis amended BLA 125297 with a second proposed proprietary name. The cover letter implied that Novartis was informed that they were required to propose a second name. In a follow-up telephone conversation on May 8, 2009, Novartis explained to OVRR that the change from Agrippal to Agriflu was a marketing decision that had very little to do with FDA's initial reservations about the name Agrippal, that the product has been licensed in Europe for at least 20 years under the name Agrippal, and that the name Agriflu would create less confusion with other flu vaccines in the US that also have the letters F-L-U in their name.

On May 7, 2009, following receipt of their April 27th CR letter, Novartis requested that FDA expedite the review of **Agriflu** and asked if it was necessary to resubmit the original proposal made on March 13, 2009, that preceded the CR letter. APLB reported to OVRR that resubmission of the proposal for the second name was unnecessary. However, we note that there has yet to be a written request to withdraw the original proprietary name proposal for Agrippal, a usual procedural step when the sponsor elects to withdraw the initial proposal that was indeed deemed to be tentatively "Acceptable."

Due to the confusion incurred by Novartis with regard to the acceptability of the original name proposal, APLB has reviewed the second proposed proprietary name, **Agriflu**.

Discussion

Agriflu is a vaccine developed for active immunization against influenza caused by virus types A (H1N1, H3N2) and B. The vaccine is proposed for use in persons 18 years of age and older, including patients with chronic underlying medical conditions.

The vaccine is intramuscular, provided as a 0.5 ml suspension for injection in pre-filled syringes (with needle) and single dose vials. Each 0.5 ml dose contains 15 µg of each of the 3 influenza strains for a total of 45 µg of hemagglutinin. The vaccine is expected to be administered by health care providers in a doctor's office, hospital, or vaccine clinic. The vaccine should be stored at 2-8°C.

- False or Misleading [21 CFR 201.6 (a)]:

  The proposed proprietary name **Agriflu** is not regarded to be false or misleading.

- Fanciful [21CFR 201.10 (c)(3)]:

The proposed proprietary name **Agriflu** is not regarded to be fanciful. It does not appear to imply that the drug or ingredient has some unique effectiveness or composition beyond that supported by the data. In addition, **Agriflu** does not encode a dosage form or regimen.

- Similarity in Spelling or Pronunciation [21 CFR 201.10 (c) (5)]:

  While the sponsor's assessment states that **Agriflu** (pronounced 'AG-gri-flew' according to the sponsor) has neither common medical suffixes or prefixes nor an incorporated generic stem (USAN) for influenza virus vaccine, **Agriflu** does, however, include the suffix "flu," as is characteristic of most of the influenza vaccines marketed in the United States at this time.

  When similarity in pronunciation and spelling (including number or similar letters) is considered**, Agriflu** has the potential to be confused with the proprietary name or established names of several drugs or products. The potential for medication errors increases with similarity in placement of letters in the names. Furthermore, since drug products are prescribed through spoken and/or electronic orders, as well as hand written prescriptions, the method of communication may lead to medication errors because of the increased potential for common spelling errors upon transcription. On the whole, **Agriflu** has a low potential for transcription error. Sound- and look-alike marketed products for **Agriflu** include those products that begin with agr- and adr-, or those products that end with -flu. Products such as Ak-fluor or Aquaphor may be a source of confusion because of the similarity of the placement of the "fu" sound following a similar velar consonant phoneme (g, k) and the sound-spelling correspondence of k and qu. There is also a potential orthographic similarity for Aquaphor with **Agriflu.** Of note, the sponsor's initial assessments of **Agriflu** showed a six- to ten-fold greater incidence of confusion (41 primary research citations for sound-alike pharmaceuticals) with **Tamiflu** than with any other candidate name when assessed for sound-alike, look-alike, and general "high probability for confusion" properties. Even with this increased potential for confusion, the overall potential for confusion remains low.

  The risk for medication errors is mitigated by indication, dosage form, storage, route of administration, and usage (home use versus health care clinic or hospital setting). **Tamiflu** is an oral dosage form and, although it is indicated for treatment of flu and prophylaxis, it has a low potential for being confused with a flu vaccine. In addition, health care professionals usually stock one brand of influenza vaccine where the product is typically referred to as "flu vaccine" rather than any specific proprietary name. For this reason, it is not of concern that **Agriflu** has a moderate potential for confusion with another flu vaccine, **Afluria**.

APLB considers the products below to have a potential for causing medication errors with **Agriflu**:

Name	Dosage Form	Rx or OTC	Dosage & Administration	Indication	Storage	Potential
Agriflu Influenza virus trivalent subunit (A/A/B hemagglutinin and neuraminidase; embryonated hen's eggs) Vaccine, Inactivated	0.5 mL suspension for injection in pre-filled syringes and single dose vials	Rx	One IM injection in patients 18 years of age and older	Influenza vaccine	2-8°C Do not freeze	N/A
Afluria Influenza virus H1N1 hemagglutinin antigen A, influenza virus H3N2 hemagglitinin antigen A, Influenza B virus antigen) Injection, suspension	0.5 mL suspension for injection in pre-filled syringes and single dose vials	Rx	One IM injection in patients 18 years of age and older	Influenza Vaccine	2-8°C Do not freeze	Moderate
Tamiflu (oseltamivir phosphate)	Capsule Powder	Rx	Oral 30, 45 and 75 mg once or twice daily 12 mg/mL	Prophylaxis and treatment of influenza	Store capsules at 25°C (77°F) Store dry powder at 25°C (77°F). Store constituted suspension under refrigeration at 2-8°C. Do not freeze.	Low to Moderate
AdreView (iobenguane I^{123}) Injection	5 mL of sterile solution for intravenous injection in a single use vial (2 mCi/mL at calibration time)	Rx	10mCi (370 MBq) IV injection over 1-2 minutes	AdreView is a diagnostic radiopharmaceutical agent for gamma-scintography used in the detection of primary or metastatic	Store AdreView at 20°-25°C (68°-77°F) excursions permitted to 15°-30°C (59°-	Low

Name	Dosage Form	Rx or OTC	Dosage & Administration	Indication	Storage	Potential
				pheochromocyt-oma or neuroblastoma as an adjunct to other diagnostic tests.	86°F). Store within the original lead container or equivalent radiation shielding.	
AK-FLUOR (fluorescein sodium) Injection for Intravenous Use	AK-FLUOR (fluorescein injection, USP) 10%, 100 mg/mL in a 5 mL single use vial. AK-FLUOR® (fluorescein injection, USP) 25%, 250 mg/mL in a 2 mL single use vial.	Rx	The normal adult dose of AK-FLUOR 10% is 5 mL (500 mg) and of AK-FLUOR® 25% is 2 mL (500 mg) via intravenous administration. For children, the dose should be calculated on the basis of 35 mg per ten pounds of body weight (7.7 mg/kg body weight).	AK-FLUOR is a diagnostic fluorescein used in angiography or angioscopy of the retina and iris vasculature.	AK-FLUOR should be stored at 20° to 25°C (68° to 77°F). Do not freeze.	Low
Aquaphor (petrolatum)	Ointment	OTC	Topical	Tx of minor skin irritations	Store at room temperature (25°C / 77°F)	Low
Agrylin (anagrelide HCl)	Capsule	Rx	Oral 0.5 mg QID	Tx of patients with thrombocythem-ia secondary to myeloprolifera-tive disorders.	Store at room temperature (25°C / 77°F) in a light resistant container.	Low

Recommendation

APLB recommends that the proposed proprietary name **Agriflu** be found "Tentatively Acceptable." If OVRR accepts our recommendation that the proposed proprietary name **Agrippal** be found tentatively acceptable, please include the following text in your letter to the manufacturer:

We have considered your proposed proprietary name **Agriflu** in consultation with CBER's Advertising and Promotional Labeling Branch (APLB) and conclude that, under 21 CFR Part 201, the proposed proprietary name is tentatively acceptable at this time.

A re-evaluation of **Agriflu** will be performed closer to the time of approval since a significant amount of time may pass between now and licensure of the product and to ensure that FDA has not approved a product with a conflicting proprietary name in the interim.

If you have any questions regarding this review please contact Lisa Stockbridge, at 301-827-3028.

References Used

- DailyMed (http://dailymed.nlm.nih.gov/dailymed/about.cfm)
- Facts and Comparisons 2009
- Drugs @ FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)
- RxList (http://www.rxlist.com/script/main/hp.asp)