

## MEMORANDUM

**From:** Marion Gruber, Director, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research

**Through:** Peter Marks, Director, Center for Biologics Evaluation and Research

**To:** BLA STN 125563/0

**Date:** December 21, 2018

**Subject:** Request from Sanofi Pasteur that FDA designate a nonproprietary name for Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine, VAXELIS, that does not include a distinguishing suffix

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**Introduction:** Sanofi Pasteur has submitted a Biologics License Application for a pediatric combination vaccine jointly developed with Merck (STN 125563, Action due December 29, 2018): Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal protein Conjugate] and Hepatitis B [Recombinant] Vaccine. The proposed proprietary name is “VAXELIS.”

The proposed indication and usage statement from the draft package insert is as follows: VAXELIS is a vaccine indicated for active immunization to prevent diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and invasive disease due to *Haemophilus influenzae* type b (Hib). VAXELIS is approved for use as a 3-dose series in children 6 weeks through 4 years of age (prior to the 5<sup>th</sup> birthday).

Other combination vaccines are approved for use in this pediatric age group; however, this is the only vaccine to cover these particular diseases.

In a July 27, 2018 communication, CBER requested that Sanofi Pasteur include a four-letter suffix in the nonproprietary name for Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal protein Conjugate] and Hepatitis B [Recombinant] Vaccine as described in the Guidance for Industry: Nonproprietary Naming of Biological Products.<sup>1</sup> The Naming Guidance recommends inclusion of a unique distinguishing suffix for biological products to facilitate pharmacovigilance “when other means to track a specific dispensed product are not readily accessible” and to “help facilitate accurate identification of these biological products by health care practitioners and patients.”<sup>2</sup> Sanofi Pasteur submitted an amendment to the BLA (dated August 3, 2018) asking the agency to reconsider the request to include a four-letter suffix on the nonproprietary name for this vaccine.

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<sup>1</sup> Guidance for Industry, Nonproprietary Naming of Biological Products (Jan. 2017) (hereinafter Naming Guidance), available at <https://www.fda.gov/downloads/drugs/guidances/ucm459987.pdf>.

<sup>2</sup> Id.at 1

Sanofi Pasteur’s amendment states that the “nonproprietary name as proposed in the draft USPI (without the suffix) is sufficient to distinguish the product, and that the addition of a suffix is unnecessary, and may potentially lead to confusion in the marketplace.” Additionally, Sanofi notes that use of a four-letter suffix may be misinterpreted as being related to the abbreviated name for this vaccine: DTaP-IPV-Hib-HepB. It is expected that this abbreviated name will be included in labeling for the vaccine. This memorandum addresses Sanofi Pasteur’s request and documents the justification for and my supervisory concurrence with the decision to depart from the recommendations in the Naming Guidance in approving a non-proprietary name without a suffix for this product.<sup>3</sup>

### **Summary:**

After reviewing the request from Sanofi Pasteur, and considering the relevant facts at hand, I have concluded that existing mechanisms to track this product are sufficient to ensure safety and pharmacovigilance and a suffix in the nonproprietary name is not necessary for the safe use of this vaccine and may have unintended negative consequences as described below.<sup>4</sup>

The issue of whether to designate the nonproprietary name of this vaccine without a distinguishing suffix was discussed with the FDA Biosimilar Implementation Committee on December 7, 2018.<sup>5</sup> The committee, including Dr. Marks and Dr. Woodcock, agreed with OVRP that a distinguishing suffix was not needed in this case and further recommended that if we designate a proper name without a distinguishing suffix for this vaccine, we should document this departure from the Naming Guidance. As Director of OVRP, I am the supervisor to OVRP staff who reviewed this BLA. This memo and documents my concurrence with the decision to depart from the Naming Guidance in this instance.

### **Consideration of the request from Sanofi Pasteur:**

The fundamental question is whether application of the naming convention described in the Naming Guidance is necessary for this vaccine, or whether other measures are in place that are sufficient to ensure safe use and pharmacovigilance in this case.

Safety monitoring for this vaccine will be accomplished through a number of programs briefly described as follows: FDA and CDC conduct safety surveillance for vaccine-associated safety concerns utilizing the Vaccine Adverse Event Reporting System (VAERS). The Vaccine Adverse Event Reporting System requests identification of the vaccine type and brand name, the manufacturer, and lot number.

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<sup>3</sup> See 21 C.F.R. § 10.115(d)(3) (“Although guidance documents do not legally bind FDA, they represent the agency’s current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence.”).

<sup>4</sup> Sanofi Pasteur made additional arguments in support of its August 3, 2018 request. However, because the Agency found it appropriate to agree with Sanofi on the grounds described in this memorandum, we do not consider or address those additional arguments.

<sup>5</sup> The CDER/CBER Biosimilars Implementation Committee is a cross-center workgroup within FDA, including Dr. Janet Woodcock and Dr. Peter Marks, that discusses issues regarding the implementation of the BPCI Act.

This system is valuable for signal detection related to a particular product. To further evaluate these signals, FDA uses the Sentinel/Post-licensure Rapid Immunization Safety Monitoring (PRISM) system which permits assessment of rates of adverse events. PRISM is a cooperative effort between FDA's CBER and its partners in health care and medical insurance companies and includes approximately 200 million patients. In addition, CDC actively monitors vaccine safety in more than 9.1 million people nationwide (over 3% of the US population) through the Vaccine Safety Datalink (VSD) project.

Analysis of a particular event post vaccination requires accurate identification of the event and the vaccine administered. For many other medical products, inclusion of a suffix in the nonproprietary name may be necessary to identify the particular biological product. For a vaccine such as VAXELIS, however, there is additional recordkeeping required that enables accurate identification of the vaccine administered without such a suffix. Specifically, the National Childhood Vaccine Injury Act of 1986 requires each healthcare provider (HCP) who administers a vaccine included in the "Vaccine Injury Table" to record in the vaccinee's permanent medical record 1) the date of administration of the vaccine, 2) the vaccine manufacturer and lot number, and 3) the name and address and, if appropriate, the title of the HCP administering the vaccine.<sup>6</sup> This requirement is unique for vaccines included in the "Vaccine Injury Table". The vaccines included in this combination vaccine are listed in the Vaccine Injury Table; when a vaccine is approved that contains a vaccine type already listed in the Vaccine Injury Table, the vaccine is automatically covered by the program.<sup>7</sup>

As noted above, we expect that the HCP will be required to document key information directly in the patient's chart, including the vaccine manufacturer and lot number, when administering this vaccine. Furthermore, additional safety monitoring programs exist for vaccines as described above. Thus, we have determined that a suffix is not needed for this particular vaccine to help facilitate the identification of the vaccine and track adverse events to a specific manufacturer, which is one of the goals of the policy described in FDA's Naming Guidance. As with all guidance documents, the Naming Guidance represents the current thinking of the Agency, and it is not binding on FDA or the public. An alternative approach may be used if it satisfies the requirements of the applicable statutes and regulations. Having considered the particular tracking requirements that a vaccine such as this one would be expected to comply with, I agree with the conclusion of OVR staff and with Sanofi that including a suffix in the proper name of this vaccine would not be necessary to advance the goals of the naming convention. Further, I agree with my staff's determination that designating a proper name with a suffix would not be necessary to meet the underlying regulatory requirements for safety for approval of this vaccine under section 351(a) of the Public Health Service Act.

**Additional considerations for this vaccine:**

An additional consideration regarding naming also applies here. As noted by Sanofi Pasteur, because the abbreviated name for this vaccine uses well-accepted, four-letter combinations of letters in a

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<sup>6</sup> <https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/vaccine-injury-table.pdf> (revised and effective March 21, 2017) (last visited December 20, 2018).

<sup>7</sup> HRSA, National Vaccine Compensation Injury Program, Frequently Asked Questions, <https://www.hrsa.gov/vaccine-compensation/FAQ/index.html> (last visited December 20, 2018)

hyphenated string, the four-letter suffix presents a risk of being mistaken by some in the public to refer to an unintended and non-specific attribute to the product as opposed to a unique distinguishing name. Some individuals may read the string of letters and believe this refers to an unidentified ingredient, a new adjuvant or an abbreviation for a chemical. This may cause confusion and concern regarding the safety of the vaccine. This confusion is particularly concerning given increased concerns by some members of the public about the safety of vaccination and rising levels of refusals by some parents to have their children vaccinated. Such confusion could undermine the effectiveness of the vaccine program overall and, ultimately, lead to negative public health effects, including outbreaks of preventable diseases and should be avoided. For all of these reasons, I concur with the decision to depart from the naming convention described in the naming guidance in this instance.

**Attachment:**

Appendix A: August 3, 2018, amendment to STN 125563 from Sanofi Pasteur



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