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| Application Type | Original BLA |
| STN | 125731/0 |
| CBER Received Date | October 8, 2020 |
| PDUFA Goal Date | June 8, 2021 |
| Division / Office | DVRPA/OVRR |
| Committee Chair | Christina Houck |
| Clinical Reviewer(s) | Tina Mongeau |
| Project Manager | Juan Lacayo, Diana Oram, Kamal Velmurugan |
| Priority Review | Yes |
| Reviewer Name(s) | Ruoxuan Xiang |
| Review Completion Date / Stamped Date | |
| Concurrence | Lei Huang Concurring Reviewer, Vaccine Evaluation Branch (VEB), Division of Biostatistics (DB), Office of Biostatistics and Epidemiology (OBE) |
| | Tsai-Lien Lin Branch Chief, VEB/DB/OBE |
| | John Scott Director, DB/OBE |
| Applicant | Pfizer Inc. |
| Established Name | 20-valent Pneumococcal Conjugate Vaccine |
| (Proposed) Trade Name | Prevnar20 |
| Pharmacologic Class | Vaccine |
| Formulation(s), including Adjuvants, etc | 2.2 µg of each of 20 saccharides, except for 4.4 µg of 6B, (b) (4) succinate buffer, (b) (4) sodium chloride, (b) (4) polysorbate 80, and 0.125 mg aluminum as aluminum phosphate |
| Dosage Form(s) and Route(s) of Administration | 0.5 mL suspension for intramuscular injection, supplied in a single-dose pre-filled syringe |
| Dosing Regimen | single dose |
| Indication(s) and Intended Population(s) | Active immunization for the prevention of pneumonia and invasive disease caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in adults 18 years of age and older |

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1. EXECUTIVE SUMMARY

1.1 Introduction

Pfizer, the applicant, submitted the original Biologics License Application (BLA) STN 125731/0 for the 20-valent Pneumococcal Conjugate Vaccine (20vPnC) completed on October 8, 2020 with rolling submissions. The vaccine is indicated for the prevention of pneumonia and invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F in adults 18 years of age and older.

20vPnC is a sterile liquid suspension for intramuscular injection, developed to expand protection against the global burden of vaccine-preventable disease caused by *Streptococcus pneumoniae* over that of currently marketed Prevnar 13 (13vPnC). 20vPnC contains the same 13 serotype-specific capsular polysaccharide antigens included in 13vPnC (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F), plus 7 additional serotype-specific capsular polysaccharides (8, 10A, 11A, 12F, 15B, 22F, and 33F). The 7 additional serotypes not covered by 13vPnC are included in the currently marketed unconjugated polysaccharide vaccine, Pneumovax 23 (PPSV23; Merck Sharp & Dohme Corp).

The clinical assay used in the three Phase 3 trials supporting this application is the opsonophagocytic activity (OPA) assay. Pfizer's OPA assays for the 13vPnC serotypes were validated previously and have been used routinely in support of 13vPnC clinical trials and for registration. The procedures for the 7 additional serotypes and for cross-reactive serotype 15C were subsequently validated and used to support Phase 3 trials. This memo focuses on the review of the validation reports of OPA assays for the 7 additional serotypes and serotype 15C. The linearity data for serotype (b) (4) is not ideal in that the (b) (4) are consistently (b) (4). However, this does not appear to have affected the non-inferiority conclusion based on immunogenicity results in the pivotal trial. The validation reports for the remaining 7 serotypes are acceptable. Therefore, I recommend approval of this BLA.

2. REGULATORY BACKGROUND

OPA assays quantitatively assess functional anti-*S pneumoniae* antibodies by measuring bacterial killing in reactions containing serially diluted test sera, baby rabbit complement, and differentiated effector cells (HL-60). The OPA titer is the reciprocal of the highest serum dilution resulting in 50% reduction in the number of bacterial colony forming units (CFUs) when compared to the control without serum (defined as the background CFU).

Pfizer's OPA assays for the 13vPnC serotypes were validated previously and have been used in support of 13vPnC clinical trials. Similar OPA assay procedures were developed and qualified for the 7 additional serotypes covered by 20vPnC and have been used in the Phase 1 and Phase 2 trials. The procedures for the 7 additional serotypes and for cross-

reactive serotype 15C were subsequently validated per the protocol to support Phase 3 trials.

3. SOURCES OF DATA AND OTHER INFORMATION CONSIDERED IN THE REVIEW

3.1 Review Strategy

The statistical review of this BLA comprises of two parts: clinical (immunogenicity and safety) data and non-clinical data. This review focuses on the non-clinical data. In particular, the validation reports of OPA assays for the 7 additional serotypes and serotype 15C are reviewed in this memo.

3.2 BLA/IND Documents That Serve as the Basis for the Statistical Review

The following submissions were reviewed:



- 125731/0.1 Module 2.7 Clinical Summary
- 125731/0.1 Module 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies
- 125731/0.5 Module 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies
- 125731/0.24 Module 1.11.3 Clinical Information Amendment

4. DISCUSSION OF INDIVIDUAL STUDIES


4.1 Method validation

The following parameters were investigated during the method validation: Dilutional Linearity; Precision; Intermediate Precision (inter-assay variability); Assay Range (LLOQ and ULOQ); and Limit of Detection (LOD).

(b) (4)



(b) (4)








5. CONCLUSIONS

(b) (4)



Therefore, the assay data can be relied upon to support approval of this BLA, as recommended in my statistical review of the clinical data.