

Application Type	Original BLA
STN	125740/0
CBER Received Date	December 15, 2020
PDUFA Goal Date	August 15, 2021
Division / Office	DVRPA/OVRR
Committee Chair	Goutam Sen
Clinical Reviewer(s)	Ihid Carneiro Leao
Project Manager	Josephine Resnick, Joseph Kulinski, Konstantin Virnik
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	Tick Borne Encephalitis Vaccine (Whole Virus, Inactivated)
(Proposed) Trade Name	Tico Vac
Pharmacologic Class	Vaccine
Formulation(s), including Adjuvants, etc	Each 0.5 mL contains sucrose gradient purified TBE virus antigen (2.4 mg target), 0.35 mg aluminum hydroxide, buffer system containing human serum albumin (HSA, 0.5 mg)
Dosage Form(s) and Route(s) of Administration	Suspension for injection in a 0.25 mL or 0.5 mL single-dose pre-filled syringe
Dosing Regimen	Three doses
Indication(s) and Intended Population(s)	For active immunization to prevent tick-borne encephalitis (TBE) in individuals 1 year of age and older

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## 1. EXECUTIVE SUMMARY

Pfizer, the applicant, submitted the original Biologics License Application (BLA) STN 125740/0 for the Tick-Borne Encephalitis Vaccine FSME-IMMUN on December 15, 2020. The proposed indication for the vaccine is prevention of tick-borne encephalitis (TBE) in individuals 1 year of age and older. The request for priority review designation was granted for this application.

As of June 2020, FSME-IMMUN has received marketing authorization in 32 countries worldwide and is currently marketed in 28 countries for the 0.5 mL presentation for individuals 16 years of age and older and 27 countries for the 0.25 mL presentation in individuals 1 through 15 years of age.

This non-clinical statistical review focuses on the in vivo potency assay. Validation of the potency assay did not include assessment of (b) (4). However, this is an in vivo potency assay and no additional experiments can be performed due to animal welfare reasons as per discussions with the product reviewers. I defer to the product reviewers on the acceptability of the in vivo potency assay.

## 2. REGULATORY BACKGROUND

On December 21, 2018, Pfizer submitted a Type C meeting request and briefing package to discuss the regulatory package to support future U.S. licensure of FSME-IMMUN.

On March 5, 2019 during the Type C meeting, it was agreed that Pfizer would open a Type 5 Master File to provide the requested data and information using the relevant sections of the Israel Marketing Authorization Application (MAA) for FSME-IMMUN.

On March 27, 2020, Pfizer submitted a Type C meeting request to discuss Chemistry, Manufacturing and Controls (CMC) aspects relevant to the Drug Substance and Drug Product manufacturing facilities and equipment to support a BLA submission for FSME-IMMUN.

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

### 3.1 Review Strategy

The statistical review of this BLA comprises two parts: clinical (immunogenicity and safety) data and non-clinical data. This review covers the non-clinical data. In particular, the in vivo potency assay is reviewed.

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

The following submissions were reviewed:

- 125740/0.0 Module 3.2.R Regional Information
- 125740/0.0 Module 3.2.P.5.3 Validation of Analytical Procedures

#### 4. DISCUSSION OF INDIVIDUAL STUDIES

##### 4.1 Method validation

(b) (4)

[Redacted text block]

(b) (4) [Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

(b) (4) [Redacted]

## 5. CONCLUSIONS

The validation of the potency assay did not include assessment of (b) (4) [Redacted]. However, this is an in vivo potency assay and no additional experiments can be performed due to animal welfare reasons as per discussions with the product reviewers. I defer to the product reviewers on the acceptability of the in vivo potency assay.