Our STN: BL 125740/0 **BLA APPROVAL**

Pfizer Ireland Pharmaceuticals August 13, 2021
Attention: Neda Aghajani Memar, Pharm.D.
235 East 42nd Street
219/9/69
New York, NY 10017

Dear Dr. Memar:

Please refer to your Biologics License Application (BLA) submitted and received December 15, 2020, under section 351(a) of the Public Health Service Act (PHS Act) for Tick-Borne Encephalitis Vaccine.

LICENSING

We have approved your BLA for Tick-Borne Encephalitis Vaccine effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Tick-Borne Encephalitis Vaccine under your existing Department of Health and Human Services U.S. License No. 2060. Tick-Borne Encephalitis Vaccine is indicated for active immunization to prevent tick-borne encephalitis (TBE) in individuals 1 year of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT00161824, NCT00161876, NCT00161785, NCT00503529, NCT01582698, NCT00161954, NCT00163540, NCT00460486, NCT00161772, NCT00161850, NCT00161863, NCT00161967, NCT00894686, NCT00840801, NCT00161798, NCT00161889, NCT00163618.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Tick-Borne Encephalitis Vaccine drug substance at (b) (4) The final formulated product will be manufactured, filled, labeled and packaged at (b) (4)

You may label your product with the proprietary name TICOVAC and market it in 0.25 mL and 0.5 mL single-dose, pre-filled syringe presentations.

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for Tick-Borne Encephalitis Vaccine shall be 30 months from the date of manufacture when stored at 5 ± 3 °C. The date of manufacture shall be defined as the date of (b) (4) Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) when stored at (b) (4)

FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of Tick-Borne Encephalitis Vaccine, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including Package Insert, submitted under amendment 31, dated August 6, 2021 and the draft carton and container labels submitted under amendment 32, dated August 10, 2021.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert, submitted on August 6, 2021. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on August 10, 2021, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125740 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80), and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines* at http://www.fda.gov/forindustry/electronicsubmissionsgateway/ucm387293.htm. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

For information on the postmarketing safety reporting requirements for combination products as described in 21 CFR 4, Subpart B, and the dates by which combination product applicants must comply with these requirements, please refer to the Postmarketing Safety Reporting for Combination Products webpage available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for the pediatric population younger than one year of age, because necessary studies are impossible or highly impracticable. This is because in TBE-endemic regions, neonates and infants are expected to have maternal antibodies that would interfere with their immune response to vaccine, while neonates and infants living in non-TBE-endemic regions cannot be ethically enrolled in a study from which there is no prospect of direct benefit.

We note that you have fulfilled the pediatric study requirement for ages 1 through 16 years for this application.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could

benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application,

Sincerely,

Marion Gruber, Ph.D.
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research