# Office of Biostatistics and Epidemiology/Division of Epidemiology
## Periodic Safety Report Review Checklist

**Completed by Reviewer**

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)</th>
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<tbody>
<tr>
<td>Manufacturer</td>
<td>Pfizer</td>
</tr>
<tr>
<td>STN #</td>
<td>19736.366</td>
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<tr>
<td>DCC Login ID #</td>
<td></td>
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<tr>
<td>Submission Type</td>
<td>PAER [ ] PSUR [ ] PBRER [ ] PADER [ ]</td>
</tr>
<tr>
<td>Submission Format</td>
<td>ELECTRONIC [✓] PAPER [ ]</td>
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<tr>
<td>Reporting Period</td>
<td>FROM April 30, 2021 TO May 31, 2021</td>
</tr>
<tr>
<td>Date Received by FDA</td>
<td>June 15, 2021</td>
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<td>Date Routed to Reviewer</td>
<td>June 15, 2021</td>
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<tr>
<td>Regulatory Information Specialist (RIS) - Name</td>
<td>Ramachandra Naik</td>
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<tr>
<td>Reviewer - Name</td>
<td>Deborah Thompson</td>
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<tr>
<td>Reviewer Signature (electronic signature)</td>
<td>Deborah L. Thompson -S</td>
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</tbody>
</table>

**COMMENTS**

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**V4_20191107_LAH**

**FDA-CBER-2021-5683-1150406**
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1. Countries where the product is licensed or authorized for distribution:
   - Not Reported □
   - US □
   - Worldwide ✔

2. Estimated number of doses distributed by reporting period/cumulative:
   - Not Reported □
   - US (b) (4) period / (b) (4) cum
   - Not Applicable □
   - Worldwide 220,976,340 period / 639,868,710 cum

3. Does this report describe any actions taken by the manufacturer or other regulatory agency for this product (e.g. labeling changes)?
   - Yes ✔
   - No □

4. Have there been any new safety issues identified by the reviewer in this PSUR?
   - Yes ✔
   - No □

If YES, please provide pertinent information below AND notify/discuss safety issues with the Team Lead and/or Branch Chief.

Safety-related changes to the Core Data Sheet include the addition of asthenia, lethargy, decreased appetite, hyperhidrosis, and night sweats as adverse drug reactions and add ion of "special warnings and precautions for use" text for vaccine stress-related responses, including dizziness, faint ing, palpitations, increases in heart rate, alterations in blood pressure, feeling short of breath, ingling sensations, swe ing and/or anxiety.

During the reporting period, the following signals were addressed by the company as follows: ongoing evaluation of myocarditis and pericarditis; appendicitis and dizziness were evaluated and determined not to be a risk. The following safety topics were addressed and determined not to be validated signals: abnormal behavior/mental disorder, acquired hemophilia, acute disseminated encephalomyelitis, acute pancreatitis, Guillain-Barre syndrome (GBS), menstrual cycle abnormalities, and transverse myelitis (TM).

A review of cumulative reports of thrombosis with thrombocytopenia syndrome (TTS) was provided; among 85 reports of potential TTS two reports met Brighton Level 1 with positive PF4 antibodies, both reports from the UK and post-1st dose (one 31-yr male with no PMH had deep vein thrombosis and platelets=135 and one 47-yr female with PMH of pulmonary embolus and concomitant anticoagulation/anti-platelet medication had cerebral venous sinus thrombosis, multiple arterial/venous thromboses, and platelets=10. The company stated that given hundreds of millions of Pfizer-BioNTech vaccine doses administered, it cannot be concluded that the vaccine is causally associated with vaccine induced thrombo ic thrombocytopenia.

Age stratified Observed to Expected (O/E) analyses showed an O/E ratio exceeding 1 for at least one age group for GBS, multisystem inflammatory syndrome, and TM; there were no trends noted across age groups. The company will continue to monitor these events.

Conclusions:
- The contents of this PSUR/PAER do not indicate a need for further regulatory action.
- Please see the following comments and recommendations:

The Information Request below was sent to the company; await response with the next Summary Monthly Safety Report. This information request (IR) is in reference to the Pfizer-BioNTech COVID-19 Vaccine Summary Monthly Safety Report (SMSR) for April 30, 2021 to May 31, 2021 (IND 19736.366) and the IR response (IND 19736.367) regarding the Observed to Expected (O/E) analysis for myocarditis and pericarditis. We acknowledge that you aim to refine the O/E analysis to provide smaller age categories for the next reporting period.

We note that in the April SMSR a myocarditis background rate of 4.4 per 100,000 person-years (py) was used for both the 18-64 year and 65+ year age groups. In the May SMSR background rates (per 100,000 py) of 12.38 for 18-24 year, 10.54 for 25-49 year, and 10.05 for 50+ year age groups were used for myocarditis based on data from ACCESS IT ARS. The ACCESS report indicates that the ARS background rates used in your O/E analysis are relatively high for myocarditis and there are a wide range of reported background rates for myocarditis. Please perform an O/E analysis for myocarditis using various background rates (i.e., lower, mid-range, and higher background rate estimates) to provide a more comprehensive range of O/E results. In addition, please perform an O/E analysis for myocarditis stratified by U.S. vs European vaccination rates (doses), age, gender, and vaccine dose. Please submit these O/E analyses for myocarditis in the SMSR for the next reporting period.

Reference Documents (X:\DE\MEDICAL OFFICER\Guidance Documents):
1. E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs 1996
2. Addendum to E2C Safety Data Management: Periodic Safety Update Reports for Marketed Drugs 2004