To:

Marco Cavaleri, Head of Biological Health Threats and Vaccines Strategy
Fergus Sweeney, Head of Clinical Studies and Manufacturing Task Force
Georgy Genov, Head of Pharmacovigilance
Juan Garcia Burgos, Head of Public and Stakeholders Engagement Department
European Medicines Agency (EMA)
Domenico Scarlattilaan 6
1083 HS Amsterdam
Netherlands

April 28, 2022

**RE: ASK-104599 - Regulatory information about safety of covid-19 vaccines –**

**I. Appeal EMA's April 13, 2022 decision letter (ASK-104599)**
**II. Request all documents on Pfizer's required post-authorisation safety study C45910153 (other study ID numbers: ClinicalTrials.gov NCT0475594, EudraCT 2020-005444-35)**

Dear Drs. Burgos, Cavaleri, Sweeney, and Genov,

We hereby appeal against your decision letter of April 13, 2022. Your response does not address the serious concerns we raised with respect to vaccine safety in pregnancy nor does it provide transparent information on your regulatory activities related to Covid-19 vaccines. The extracted information you provided from the EudraVigilance database based on the EudraCT numbers alone is misleading, incomplete, and inconsistent with other SAE data available on Pfizer's pivotal trial on Comirnaty (C4591001, NCT04368728, or EudraCT number 2020-002641-42, respectively).[1,2]

The information you provided for the ongoing Pfizer and Moderna post-authorisation pregnancy trials is also insufficient.

Firstly, as the Risk Management Plan for Elasomeran (Spikevax) [3] clearly shows, study NCT04958304 (mRNA-1273-P902) is to be conducted in the US, Canada, and the EU. Therefore, regular 6 month reporting in Periodic Safety Update Reports (PSURs) to the PRAC and CHMP is mandatory, according to EMA's "exceptional transparency" rules.

Secondly, in your reply of February 14, 2022, you answered:

> *EMA has not been informed of any problems with recruitment with the trials. The study identifier is the identifier used by clinical trials.gov. We understand that study NCT04754594 corresponds to EudraCT number 2020-005444-35. This study is a post authorisation study that is currently ongoing to specifically monitor the safety in pregnant women who received the vaccine and is one of several ongoing studies.*

> *As the supervision of clinical studies is within the remit of the national competent authorities EMA cannot comment on the reason behind any protocol changes for a study it has not yet assessed.*

In your letter of April 1, you repeated contending that you do not hold this information:

> *EMA cannot comment on the reason behind any protocol changes for a study it has not yet assessed; once the company submits data from the clinical trial in question to EMA, it will be evaluated by EMA's scientific committees.*

The BNT162b2 Risk Management Plan Update of February 2022 [4] suggests that you already held the requested information by the time of your first reply but preferred not to disclose it.

See "Module SIII. Clinical Trial Exposure: Addition of final enrollment numbers of study C4591015":

> *A phase 2/3 placebo-controlled, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older. A total of 348 (209 in phase 2 and 139 in phase 3) pregnant women at 24 to 34 weeks gestation were randomised in a 1:1 ratio to vaccine or placebo. Enrollment of participants into study C4591015 was stopped on 25 October 2021 due to recruitment challenges as a result of global recommendations for COVID-19 vaccination in pregnant women and the increased availability of COVID-19 vaccines. Participants already enrolled will continue follow up evaluations until study end as planned.*

Of note, the study was originally planned to enroll 4000 pregnant women. Stopping the trial at an enrollment of 348 participants (less than 10% of the intended study size) means that no meaningful results will be obtainable from this trial. Complete documentation of why this trial terminated should be available. It is of highest public interest to disclose the reasons for the protocol changes/violations in study C4591015 (other study ID numbers include ClinicalTrials.gov NCT04754594 and EudraCT number 2020-005444-35).

**Clarification of freedom of information request**

Following the advice of the European Ombudsman, we hereby clarify that our request (ASK-104599) includes an **access to documents request for all documents relate**d to study C4591015 (ClinicalTrials.gov number NCT0475594 and EudraCT number 2020-005444-35). Our request includes, but is not limited to:

- anonymized individual participant data (IPD) of all trial participants from the time of screening (i.e. before randomisation), through group allocation (vaccine versus placebo) and follow-up, explicitly including those women who withdrew (or were withdrawn) after receiving only one dose
- all respective case report forms (CRFs)

- all Periodic Safety Update Reports (PSURs) and Periodic Safety Update Reports Single Assessments (PSUSAs) (e.g. PSUSA/00010898/202112, PSUSA/00010898/202206, and following)
- all requests for supplementary information
- PRAC Rapporteur's preliminary AR EMEA/H/C/005735/II/0087
- any other documentation submitted to or issued by EMA based on the original RMP and all subsequent RMP revisions.

Yours sincerely,

Ulrich Keil, MD, PhD, FRCP, University of Münster

Angela Spelsberg, MD, Comprehensive Cancer Centre, Aachen

References:

[1] https://phmpt.org/pfizers-documents/

[2] Bridle BW, Martins I, Mallard BA, Karrow NA, Speicher DJ, Chaufan C, Northey, JGB, Pelech S, Shaw CA, Halgas O, McLeod D. Concerns regarding the efficacy and safety for BNT162b2 mRNA coronavirus disease (COVID-19) vaccine through six months. www.CanadianCovidCareAlliance.org (January 10, 2022) 1-10, accessed April 18, 2022.

[3] https://www.ema.europa.eu/en/documents/rmp-summary/spikevax-previously-covid-19-vaccine-moderna-epar-risk-management-plan_en.pdf

[4] https://www.ema.europa.eu/en/documents/rmp-summary/comirnaty-epar-risk-management-plan_en.pdf