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)

European Medicines Agency (EMA)
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The Netherlands

Request to obtain regulatory information about safety of Covid-19 vaccines around conception and during pregnancy by European members of the Coalition Advocating for Adequately Licensed Medicines

Münster, January 11, 2021

Dear Drs. Cavaleri, Sweeney, and Genov,

We are writing to you for inquiring about safety data from post-authorisation studies required by the European Medicines Agency. As detailed in our Citizen Petition (Docket Number: FDA-2021-P-0786), [1] the pivotal phase 3 trials of COVID-19 mRNA vaccines largely (or wholly) excluded the following important populations in which there is reason to believe the effects of the product may differ from the populations enrolled in the trial. For example: newborn infants and small children, individuals with past SARS-CoV-2 infection or with immunosuppression, persons with history of or current cancer, hematological disorders, or autoimmune diseases, as well as frail older adults (including those living in nursing homes) and pregnant or nursing women.

Covid-19 vaccines are the most recent and prominent example of expedited regulatory approval. [2] Among the 21 post-authorisation studies mandated by EMA before granting conditional authorisation to mRNA vaccines, two are addressing safety of vaccination during pregnancy. Although preliminary analyses of the CDC v-safe and US Vaccine Adverse Event Reporting System (VAERS) data were interpreted as showing no safety concerns of COVID-19 mRNA vaccines for pregnant women, [3,4] an increased risk of adverse pregnancy outcomes, particularly if mRNA vaccines are administered around conception up to 20 weeks of gestation, cannot be excluded. [5]

Just one required randomized controlled trial in pregnant women is being conducted by Pfizer-BioNTech (***NCT04754594,*** *registered on February 15, 2021*). The history of changes on ClinicalTrials.gov shows the study originally planned to enroll 4000 women at 44 different sites in the U.S., but by June 16, 2021, the number of participants was reduced to only 700 women. Surprisingly, since November 16, 2021, the registered trial status has changed to “active, not recruiting” at an actual enrollment of only 343 participants. [6] This is alarming. In addition, NCT04754594 also involves four study sites run by Ventavia, the company working on Pfizer’s primary pivotal trial recently disclosed to have major problems with quality assurance and data handling. [7] Importantly, the study only enrolls women 24 to 34 weeks pregnant, and thus cannot address questions regarding how the vaccine may adversely affect outcomes around conception and during early pregnancy.

We ask you, as EMA representatives:

1. To disclose whether you are aware of these protocol changes/violations. If yes, we ask EMA to swiftly inform the public whether you approved the changes and to provide the reasons behind these changes.
2. To inform the public what EMA has done in terms of oversight, in response to specific reports of data integrity problems at clinical trial sites operated by Ventavia, as well as provide a report similar to the FDA BIMO report, [8] indicating which clinical trial sites from trial ***NCT04754594 and NCT04368728*** EMA has inspected, and the outcome of the inspections.
3. Did you receive severe adverse events (SAE) reports and if so, how many reports about miscarriages, fetal or maternal deaths, fetal malformation, intrauterine disease, growth anomalies, premature births, complicated pregnancies or any other severe adverse events from ***NCT04754594*** *or* Pfizer's pivotal trial ***NCT04368728*** among vaccinated pregnant women (including information on week of pregnancy)?
4. Have you been informed about problems with recruitment of study participants which obviously persisted even after doubling recruitment sites from originally 44 sites in the U.S. to roughly 100 sites also abroad (South Africa, Spain, UK) by June 2021?

The risk management plan for the conditionally approved Moderna mRNA vaccine lists an observational cohort study (**NCT04958304**) started in July 2021, which will follow 1000 pregnant women from day 28 after last menstrual period up to one year after termination of pregnancy. [9] Given the small sample size and a marked potential for selection bias of study participants, statistical power and chances of detecting adverse events during early pregnancy are extremely low. Nevertheless, we ask:

5. Did you receive any SAE reports from this study (NCT04958304)?

Calls for covid-19 vaccine mandates for the general population or imposing them on specific groups such as health care workers or other "exposed" professionals must be weighed against not only the known but also the unknown risks that the novel covid-19 vaccines may bear. [10] This is particularly the case when we are seeing, in risk-benefit analyses at least in the US and perhaps in Europe, that unproven-but-assumed benefits (such as a durable reduction in risk of serious disease over time) are being factored into regulatory decision making.

In the best public interest, we urge EMA to immediately disclose available safety data concerning the health of expecting mothers and their children from the pivotal trials and the respective mandated post-marketing studies of Covid-19 mRNA vaccines. If EMA is not able to present reliable safety data on Covid-19 vaccination around conception and during pregnancy, political decision makers put the global community at very high risk of irreversible damage if they go for Covid-19 vaccine mandates.

Please be reminded that the thalidomide catastrophe of the late 1950s to 1962 [11] was largely attributable to the scientifically unproven reassurance of doctors to their patients that the new drug was particularly designed to be safe for pregnant women. Good intentions are not enough. We therefore demand as physicians and EU citizens in the highest public interest that transparent and scientifically sound information is provided immediately by regulators about the availability of safety data around conception and during pregnancy from Covid-19 vaccine trials as well as mandated post-authorisation studies before coercing vaccination to individuals who want to have children, as well as pregnant or nursing women and to their infants.

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References:

[1] https://downloads.regulations.gov/FDA-2021-P-0786-0001/attachment_1.pdf

[2] Pruger C., et al. Evaluating covid-19 vaccine efficacy and safety in the post-authorisation phase. *BMJ 2021;375:e067570*

[3] Shimbakuro,TT, Kim SY. Et al. Preliminary findings of Covid-19 mRNA vaccine safety in pregnant persons. NEJM 384(24):2273-82
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[4] Shimbakuro,TT, Kim SY. Et al. Preliminary findings of Covid-19 mRNA vaccine safety in pregnant persons. corrected version NEJM 384(24):2342-43
https://www.nejm.org/doi/full/10.1056/NEJMx210016

[5] Karrow, N.A.; Shandilya,U.K.; et al. Maternal COVID-19 Vaccination
and its potential impact on fetal and neonatal Development. Vaccines 2021;9,1351.
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[6] https://clinicaltrials.gov/ct2/show/NCT04754594?term=NCT04754594&draw=2&rank=1

[7] Thacker PD. Covid-19: Researcher blows the whistle on data integrity issues in Pfizer's vaccine trial. *BMJ 2021; 375:n2635 doi: https://doi.org/10.1136/bmj.n2635*

[8] https://www.fda.gov/media/153947/download

[9] https://clinicaltrials.gov/ct2/show/NCT04958304?term=NCT04958304&draw=2&rank=1

[10] Kmietovicz Z. Evidence is insufficient to back mandatory NHS staff vaccination, says House of Lords committee. BMJ 2021;375:n2957 *https://doi.org/10.1136/bmj.n2957*
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[11] Vargesson N. 2015. Thalidomide-induced teratogenesis: History and mechanisms. Birth Defects Research (Part C) 105(2): 140–56. doi: 10.1002/bdrc.21096.