Parlement européen

Madam Emer Cooke
Executive Director
European Medicines Agency

Brussels, 16th November 2021

Subject : Integrity of clinical data, Additional clinical trials and studies, Pharmacovigilance and mRNA Covid-19 Vaccine Safety

Dear Madam Cooke,

With this letter, we wish to address a number of key questions concerning the research and the assessment related to mRNA COVID-19 vaccines. We hope to receive precise answers from you within a reasonable timeframe.

A. Additional, booster or extra, doses

On October 4th 2021, EMA's human medicines committee (CHMP) announced that an extra dose of the COVID-19 vaccines Comirnaty (BioNTech/Pfizer) and Spikevax (Moderna) may be given to people with severely weakened immune systems, at least 28 days after their second dose.

The recommendation came after studies – references are given by EMA – showed that an extra dose of these vaccines increased the ability to produce antibodies against the virus that causes COVID-19 in organ transplant patients with weakened immune systems. *"Although there is no direct evidence that the ability to produce antibodies in these patients protected against COVID-19, it is expected that the extra dose would increase protection at least in some patients,"* the agency declared[1].

On the basis of the data provided by Pfizer/BioNtech application for Comirnaty, the EMA stressed that the CHMP concluded that booster doses may be considered at least 6 months after the second dose for people aged 18 years and older. In addition, on September 27th, the EMA has started evaluating an application for the use of a booster dose of Spikevax to be given at least 6 months after the second dose in people aged 12 years and older. On Oct. 25th, EMA's CHMP concluded that a booster dose of Spikevax may also be considered in adults at least six months after the second dose.

The EMA makes a clear distinction between the additional dose for immunocompromised persons and booster doses for persons with normal immune systems. *"Although the EMA and ECDC do not consider the need for booster doses of COVID-19 vaccine to be urgent in the general population, the EMA is assessing this application to ensure that evidence is available to support additional doses if necessary,"* said the EMA in its 27 September press release.

1 Comirnaty and Spikevax: EMA recommendations on extra doses and boosters. 4 oct 2021 https://www.ema.europa.eu/en/news/comirnaty-spikevax-ema-recommendations-extra-doses-boosters

Therefore, we would like to ask:

1. What are the additional data and studies on which the EMA has based its recommendations for additional, booster or extra doses, applications to extend the use made by manufacturers Pfizer and Moderna for their respective mRNA vaccines?

2. How to access these studies and data? When will they be publicly available?

B. Flawed clinical data for Comirnaty vaccine, exposed by the BMJ

On 2 November 2021, the *British Medical Journal* (BMJ) reported on the fraudulent clinical trial committed by a Pfizer's subcontractor: Ventavia Research Group. Poor practices at this Texas-based privately owned clinical research company helping to carry out Pfizer's pivotal covid-19 Comirnaty vaccine trial raise questions about data integrity. The devastating investigation of the *BMJ* reveals especially how the company falsified data, unblinded patients, employed inadequately trained vaccinators, and was slow to follow up on adverse events reported in Pfizer's pivotal phase III trial[2].

In addition to the unreported adverse events, fake double-blinding was reported: Ventavia investigators wera able to know who had received the vaccine or placebo, which may have allowed them to select patients for PCR testing from those with Covid symptoms in the vaccine or placebo groups. The FDA was alerted on the unsound practices but did not investigate, and the whistleblower was fired. Since irregularities have been reported in September 2020, Pfizer has hired Ventavia as a research subcontractor on four other vaccine clinical trials (including three on covid-19 vaccine in children and young adults, pregnant women, and a booster dose).

The full Comirnaty clinical trial of Pfizer enrolled around 44 000 participants across 153 sites that included numerous commercial companies and academic centres. Pfizer reported 170 PCR confirmed covid-19 cases, split 8 to 162 between vaccine and placebo groups.

The *BMJ* has already described how the protocol for clinical trials of mRNA vaccines was not designed to test their effectiveness against infection[3]. But there are other concerns about the quality of the clinical data provided by Pfizer. According to FDA's report on Pfizer's vaccine, there were *"3410 total cases of suspected, but unconfirmed covid-19 in the overall study population, 1594 occurred in the vaccine group vs. 1816 in the placebo group"* stated Peter Doshi, one the editors of the BMJ. Since January 2021, Peter Doshi required access to the raw trial data complaining that if we included the "suspected covid-cases", a rough estimate of vaccine efficacy against developing covid-19 symptoms, with or without a positive PCR test result, would be a relative risk reduction of 19% — far below the "95% effective" claims from Pfizer[4].

The Pfizer's preprint article, released on July 28th 2021, provided no additional data on vaccine efficacy beyond six months, and was only based on 7% of trial participants: the ones who actually reached six months of blinded follow-up[5]. *"It is hard to imagine that the <10% of trial participants who remained blinded at six months could constitute a reliable or valid sample to produce further*

2 Thacker P D. Covid-19: Researcher blows the whistle on data integrity issues in Pfizer's vaccine trial BMJ 2021; 375 https://www.bmj.com/content/375/bmj.n2635 (Published 02 November 2021)

3 Doshi P. Will covid-19 vaccines save lives? Current trials aren't designed to tell us BMJ 2020; 371 www.bmj.com/content/371/bmj.m4037

4 Peter Doshi : Pfizer and Moderna's "95% effective" vaccines—we need more details and the raw data, 4 janv 2021 https://blogs.bmj.com/bmj/2021/01/04/peter-doshi-pfizer-and-modernas-95-effective-vaccines-we-need-more-details-and-the-raw-data/

5 Six Month Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine https://www.medrxiv.org/content/10.1101/2021.07.28.21261159v1

findings" wrote Peter Doshi[6]. *"In the preprint, high efficacy against "severe covid-19" is reported based on all follow-up time, but the number of hospital admissions is not reported so we don't know which, if any, of these patients were ill enough to require hospital treatment"* also noted the senior editor. A two-year clinical trial is still ongoing; no new additional data were released since March 2021; unclear efficacy with evidence of waning protection after a few months, limited reporting of efficacy and safety data… The *BMJ*'s analysis of the Comirnaty clinical data raises many questions.

3. Has the EMA been given access to adequate, complete raw data from Pfizer's Comirnaty clinical trials? Are those data publicly available?

4. Has this raw data been analysed by experts independent of Pfizer?

5. How has the EMA ensured that the data provided by the company is verified?

6. Has the EMA been informed of any irregularities reported during the Phase 3 clinical trial coordinated by Ventavia?

7. Will the EMA review its assessment of Comirnaty in the light of these new data and the comments made by the BMJ?

C. Suspension of the use of Moderna's Spikevax for males under the age of 30 in October 2021 by Finland, Sweden, Norway and Denmark

At national level, public health bodies may issue official recommendations on the use of booster doses, taking into account emerging effectiveness data and the limited safety data.

"The risk of inflammatory heart conditions or other very rare side effects after a booster is not known and is being carefully monitored. As for all medicines, EMA will continue to look at all data on the safety and effectiveness of the vaccine" stated the EMA in its October 4th news.

On October 7th, Finland paused the use of Spikevax vaccine for younger males due to reports of a rare cardiovascular side effect joining Sweden, Norway and Denmark, Iceland followed on Oct. 8th, limiting its use to men aged 12 and over.

"A Nordic study involving Finland, Sweden, Norway and Denmark found that men under the age of 30 who received Moderna Spikevax had a slightly higher risk than others of developing myocarditis," said Mika Salminen, director of the Finnish health institute[7]. The Finnish institute of Health said the Nordic study would be published within a couple of weeks and preliminary data – similar to the ones previously posted in April 2021 by Israel which have started with the Comirnaty the vaccination of the 16-18 years old since January 2021[8] ; or from Canada, which stated on August 27th 2021 that myocarditis and pericarditis occured two and a half times more frequently among those who received the Moderna vaccine than in those who had received Pfizer[9] – had been sent to the EMA for further assessment.

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6 Peter Doshi : Does the FDA think these data justify the first full approval of a covid-19 vaccine? 23 Aug 2021 https://blogs.bmj.com/bmj/2021/08/23/does-the-fda-think-these-data-justify-the-first-full-approval-of-a-covid-19-vaccine/

7 Reuters : Finland joins Sweden and Denmark in limiting Moderna COVID-19 vaccine. 7 oct 2021 https://www.reuters.com/world/europe/finland-pauses-use-moderna-covid-19-vaccine-young-men-2021-10-07/

8 Israel Ministry of Health. Surveillance of Myocarditis (Inflammation of the Heart Muscle) Cases Between December 2020 and May 2021 (Including). 2 June 2021. https://www.gov.il/en/departments/news/01062021-03

9 Summary of National Advisory Committee on Immunization (NACI) statement: recommendation on the use of mRNA covid-19 vaccines in adolescents 12 to 17 years of age.27 August 2021. www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/mrna-adolescents/summary.html

In the United States, the Food and Drug Administration (FDA) approved Pfizer-BioNTech's COVID-19 vaccine for emergency use in children aged 5 to 11 years on 29 October 2021. But the US emergency use authorisation of Moderna's coronavirus vaccine in people aged 12-17 will be delayed, reported the *British Medical Journal* on Nov. 1st[10]. Moderna said it will also delay its application for authorisation in 6-11 year olds. The FDA warned the company that the authorisation in 12-17 year old could now take until January 2022, informing that it "requires additional time to evaluate recent international analyses of the risk of myocarditis after vaccination" stated Moderna in a press briefing on Oct. 31th[11].

France advises against the injection of Moderna mRNA vaccine in people under 30 years of age as of 8 November

In France, the Haute Autorité de Santé (HAS) first advised on Oct. 6th to use Pfizer's Comirnaty in case of a 3rd dose injection. Then, after learning of risks from Scandinavian countries, on Oct. 15th the HAS explicitly recommended suspending booster injections with the Moderna vaccine. *"The announcements by various health authorities have highlighted the unknowns that remain concerning the dose and target population for the Spikevax® (Moderna) booster and justify waiting for the European authority to provide the expected clarifications in the context of the MA currently under review,"* wrote the HAS[12].

On November 8th, the Agence Nationale de Sécurité du Médicament (ANSM) and the Caisse Nationale d'Assurance Maladie (CNAM) published the latest data from the Epi-pharmaco-epidemiology study Epi-Phare on the risk of myocarditis and pericarditis with mRNA vaccines in subjects aged 12 to 50 years in France. This study confirms the existence of an infrequent risk of myocarditis and pericarditis in the 7 days following vaccination against Covid-19 with an mRNA vaccine (Comirnaty and Spikevax) in people aged 12 to 50 years, particularly in young people aged 12 to 29 years.

These risks of heart inflammation are higher with Moderna's Spikevax vaccine, the French authorities noted. Although "very rare" and "with a favourable outcome", this risk of myocarditis appears to be about 5 times higher in people under 30 with the Spikevax vaccine. In men, *"vaccination with Spikevax would be the cause of 132 additional cases of myocarditis per million doses administered"* (compared to an excess of 27 cases per million in the case of vaccination with Comirnaty), and *"the excess of cases attributable to the second dose of Spikevax would be of the order of 37 per million doses"* in young women under 30 years of age, the ANSM press release stated[13]. In people under 30, particularly after the second dose, Spikevax vaccine would also be responsible for an excess of 18 cases of pericarditis per million doses.

Following these results, the HAS recommended on the same day, 8th November, that the Moderna vaccine (Spikevax) should not be used in France in children and adults under 30 years of age, either as a primary vaccination or as a booster dose (half dose)[14].

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10 Dyer O. Covid-19: FDA puts Moderna's paediatric application on hold to investigate side effects. BMJ 2021; 375 (Published 01 Nov. 2021) doi: https://doi.org/10.1136/bmj.n2659

11 Moderna Provides Update on Timing of U.S. Emergency Use Authorization of its COVID-19 Vaccine for Adolescents, 31 oct 2021 https://investors.modernatx.com/news-releases/news-release-details/moderna-provides-update-timing-us-emergency-use-authorization/

12 HAS. Covid-19 : utiliser le vaccin de Pfizer pour le rappel de vaccination, 15 oct. 2021 https://www.has-sante.fr/jcms/p_3292786/fr/covid-19-utiliser-le-vaccin-de-pfizer-pour-le-rappel-de-vaccination

13 Le risque de myocardite et péricardite après la vaccination Covid-19 est confirmé mais peu fréquent et d'évolution favorable, ANSM, 8 nov. 2021 https://ansm.sante.fr/actualites/le-risque-de-myocardite-et-pericardite-apres-la-vaccination-covid-19-est-confirme-mais-peu-frequent-et-devolution-favorable

14 Covid-19 : la HAS précise la place de Spikevax dans la stratégie vaccinale, 8 nov. 2021 https://www.has-sante.fr/jcms/p_3297260/fr/covid-19-la-has-precise-la-place-de-spikevax-dans-la-strategie-vaccinale

EMA's safety committee asks Pfizer and Moderna to perform an in-depth review of all published data on the association of myocarditis and pericarditis

Now that the frequency of possible risks of myocarditis and pericarditis inflammation have been observed in different countries in people who have received at least one dose of an mRNA vaccine, and that the frequency of their risk of occurrence after an injection of the Comirnaty or Spikevax vaccines also seems to be better known, what is now the EMA's position on these mRNA vaccines?

On Oct. 18th 2021, EMA started evaluating an application to extend the use of BioNTech/Pfizer's COVID-19 vaccine Comirnaty, to include children aged 5 to 11[15]. The Comirnaty Conditional marketing authorisation has been issued on December 21th 2020, extended to use in individuals aged 12 years and older on 31 May 2021, but its annual renewal has been given on 3 Nov. 2021[16].

Moderna's COVID-19 Spikevax is a vaccine that was authorised in the EU on January 6th 2021, its annual renewal has been issued on Oct. 4th 2021[17]. Three months ago, on 23th July 2021, the conditional marketing authorisation was extended to use in individuals aged 12 years and older. On November 10th, EMA has started evaluating an application to extend the use of vaccine Spikevax to children aged 6 to 11[18].

On the risk of myocarditis and pericarditis following vaccination, on October 29th, 2021, the EMA's safety committee (PRAC) asked the companies that market these Spikevax and Comirnaty mRNA vaccines *"to perform an in-depth review of all published data on the association of myocarditis and pericarditis, including clinical trial data, data from the literature and data available in the public domain".*

Moderna said in its statement on Oct. 31th, that *"to date, the observed rate of myocarditis reports in those less than 18 years of age in Moderna's global safety database does not suggest an increased risk of myocarditis in this population."* But, the company added, it *"does not yet have access to data from some recent international analyses."* In its latest brief conference, on 11th Nov., Moderna ackowledged a slightly increased risk of myocarditis when compared to the Pfizer-BioNTech vaccine. *"This applies to primary vaccination, not booster, and has not been observed in females. Testosterone may be a contributory factor"*[19]. Two weeks ago, on Oct 25th, Moderna says COVID-19 vaccine for kids under 12 showed strong results, without details on the adverse events reported[20].

The serious concerns about the quality of the data and the ability of mRNA vaccine manufacturers to provide a safe, objective and unbiased assessment

The evidence gathered in this letter shows that important questions still remain. There are currently different benefit/risk assessments of Pfizer and Moderna mRNA vaccines. In the case of Comirnaty, there are serious doubts about the quality of the data used by Pfizer to conclude that its vaccine is effective. The lack of convincing answers from Pfizer does not dispel fears of falsification of clinical trial data submitted to the FDA or the EMA.

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15 https://www.ema.europa.eu/en/news/ema-starts-evaluating-use-covid-19-vaccine-comirnaty-children-aged-5-11

16 https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-comirnaty-11-november-2021_en.pdf

17 https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised

18 EMA starts evaluating use of COVID-19 vaccine Spikevax in children aged 6 to 11. 10 nov 2021 https://www.ema.europa.eu/en/news/ema-starts-evaluating-use-covid-19-vaccine-spikevax-children-aged-6-11

19 Moderna notes higher myocarditis risk for young males when compared to Pfizer's vaccine, 11 Nov 2021 https://endpts.com/covid-19-roundup-moderna-notes-higher-myocarditis-risk-for-young-males-when-compared-to-pfizers-vaccine-ema-signs-off-on-roche-celltrion-mab-treatments/

20 https://fortune.com/2021/10/25/moderna-covid-19-vaccine-kids-under-12-strong-results-data

For Moderna's Spikevax vaccine, several European national authorities believe that the increased risk of post-vaccination myocarditis and pericarditis is now sufficiently established to suspend and advise against the use of Moderna's vaccine in people under 30 years of age, particularly in boys. At the same time, the EMA is making almost the opposite assessment: initiating a review of applications to extend the use of Pfizer's and Moderna's vaccines to children aged 5-11 years; and requesting Pfizer and Moderna to conduct a thorough review of all published data on the risk of myocarditis and pericarditis following mRNA vaccination.

However, many questions remains:

8. To date, how many cases of myocarditis and pericarditis were reported after injections in under-30s of Moderna's vaccine, and to a lesser extent Pfizer's? How many cases and studies will be needed before the EMA revises its position and follows the precautionary recommendations already made in 4 EU countries?

9. Why did the EMA not take the initiative of an emergency plan, including active pharmacovigilance, on the under-30s vaccinated with Comirnaty or Spikevax, in order to have reinforced data? And why, instead of entrusting this analysis to Pfizer or Moderna, does the EMA not carry out its own in-depth analysis of the data already published or collected by the laboratories or the national authorities?

10. Does the EMA realize that by asking Pfizer and Moderna to carry out this in-depth analysis, the EMA is placing these companies in a conflict of interest situation?

11. How can we take into account the fact that the two companies Pfizer and Moderna, which have filed applications in the United States and the European Union to extend the authorisation of their vaccines for 5-11 year old, have a direct commercial and financial interest in minimising the risks of myocarditis and pericarditis that can occur in these youngest populations?

12. How can this in-depth analysis be complete and objective when the post-vaccination surveillance data from the Scandinavian study - which were sent to the EMA at the beginning of October - have not yet been made public?

13. How, in these circumstances, does the EMA plan to verify and ensure the quality and integrity of the extensive data analysis requested from Pfizer and Moderna? What are the EMA's safeguards to ensure the data are legitimate and accurate? Does the EMA request any additional independent studies on this issue?

14. Will these in-depth analyses be provided to the EMA before its decision on the extension of the use of BioNTech/Pfizer's Comirnaty and Moderna's Spikevax COVID-19 vaccines for children aged 5-11 years?

15. Will these in-depth studies and their data be publicly available?

The lack of reliable existing data, the discrepancies found and the risks highlighted show that the clinical trials and post-vaccination monitoring carried out by the vaccine manufacturers alone are not sufficient.

The decisions taken by the health authorities of several Member States regarding the vaccination of the youngest children with the Moderna vaccine, for example, show that it is no longer possible to continue "business-as-usual" and act as if nothing had happened.

Our letter raises many essential questions. A true and robust European Health Union needs to be built on trust and transparency. We expect from you and the EMA precise responses which will contribute to, above all, the high level of human health protection that shall be ensured in Europe.

Thanks you very much in advance,

Sincerely,

MEP Michele Rivasi
MEP Piernicola Pedicini
MEP Tilly Metz