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European Medicines Agency

Dear Honourable Members of Parliament Marcel de Graaff, Joachim Kuhs, Virginie Joron, and Bernhard Zimniok,

Subject: Response to your letter dated 1 December 2023

Thank you for your letter of 1 December 2023 in which you request clarification concerning our reply to your letter of 4 October 2023.

In your initial letter you called for the immediate suspension of the marketing authorisations of Comirnaty and Spikevax. In our reply, we explained the basis of the authorisation of these vaccines and why any such suspension would be a great disservice to public health.

Despite the end of the public health emergency and the higher levels of immunity in the population, SARS-CoV-2 variants continue to spread in Europe and other parts of the world. Vaccination is an essential tool for protecting people against COVID-19, particularly those at high risk of severe disease.

Please find below responses to the questions you raise in your follow-up letter.

1. Transmission prevention

   In reply to your first letter, we responded to a question about the authorisation of mRNA vaccines by stating that the vaccines are only authorised for protecting the vaccinated person against disease.

   It appears the implications of the statement were misconstrued. In general, vaccines are authorised by medicines regulators to protect vaccinated individuals against a disease, but this does not mean that they cannot be used with an *additional* aim of reducing transmission. Depending on the disease, national authorities have historically considered potential additional benefits of vaccination.

   In dealing with infectious diseases, national authorities also consider the epidemiological situation, including infection rates and the burden of the disease, especially in vulnerable groups.

   Please note that national vaccination strategies fall outside the remit of EMA.

With respect to COVID-19, at the beginning of the pandemic, regulators asked companies to prioritise studies looking at how well the COVID-19 vaccines protected against the disease, because measuring how well they reduce transmission of SARS-CoV-2 is difficult in clinical studies. The latter can only be measured in real-world studies that include large numbers of vaccinated people, and these were not available at the time of initial authorisation of the vaccines.

Several studies carried out after their authorisation have since shown that COVID-19 vaccines can reduce the transmission of the virus.[1,2,3,4,5,6,7] However with the emergence of more transmissible SARS-CoV-2 variants and with waning immunity, it has been more difficult to quantify this effect for the different variants.

2. Informed consent

Under the heading 'informed consent', you raise a number of questions about vaccination policy. We would refer you to the above observations regarding the role of national authorities and highlight that EMA is not responsible for running mass vaccination campaigns or training personnel to administer vaccines.

We would also like to point out that information on side effects is included in the summaries of product characteristics (SmPCs) and package leaflets covering the full authorised use of the vaccine concerned. While there are now many adapted vaccines authorised, the SmPC text for each vaccine is comprehensive. Contrary to your claim, there is no legal requirement for separate documents for boosters.

You also state that 'information about the restricted marketing authorisation was also very poorly disseminated.' We assume you are referring to conditional marketing authorisations (CMAs). If so, please note that EMA communicated extensively about CMAs on its website, in public stakeholder meetings and during press briefings. We were clear about the fact that the marketing authorisations were conditional and about the conditions for converting the CMAs to standard marketing authorisations. Indeed information on the conditional status of the authorisation was in the package leaflets and the summaries of product characteristics.

We also do not agree with your characterization of the vaccines as 'experimental' medicines. A CMA is only granted if the evidence shows that the benefits outweigh the risks. It is one of the EU's regulatory mechanisms for facilitating early access to medicines that fulfil an unmet medical need, including in emergency situations such as the COVID-19 pandemic. The studies supporting the initial marketing authorisations were among the largest ever pre-approval trials conducted for vaccines, and data obtained since authorisation have confirmed their benefits and safety.

[1] Regev-Yochay G, Amit S, Bergwerk M, et al. Decreased infectivity following BNT162b2 vaccination: A prospective cohort study in Israel. Lancet Reg Health Eur. 2021;7:100150. doi:10.1016/j.lanepe.2021.100150
[2] Prunas O, Warren JL, Crawford FW, et al. Vaccination with BNT162b2 reduces transmission of SARS-CoV-2 to household contacts in Israel. Science. 2022;375(6585):1151-1154. doi:10.1126/science.abl4292
[3] Tan ST, Kwan AT, Rodríguez-Barraquer I, et al. Infectiousness of SARS-CoV-2 breakthrough infections and reinfections during the Omicron wave. Preprint. medRxiv. 2022;2022.08.08.22278547. Published 2022 Nov 21. doi:10.1101/2022.08.08.22278547
[4] Richterman A, Meyerowitz EA, Cevik M. Indirect Protection by Reducing Transmission: Ending the Pandemic With Severe Acute Respiratory Syndrome Coronavirus 2 Vaccination. Open Forum Infect Dis. 2021;9(2):ofab259. Published 2021 May 19. doi:10.1093/ofid/ofab259
[5] Braeye T, Catteau L, Brondeel R, et al. Vaccine effectiveness against transmission of alpha, delta and omicron SARS-COV-2-infection, Belgian contact tracing, 2021-2022. Vaccine. 2023;41(20):3292-3300. doi:10.1016/j.vaccine.2023.03.069
[6] Mongin D, Bürgisser N, Laurie G, et al. Effect of SARS-CoV-2 prior infection and mRNA vaccination on contagiousness and susceptibility to infection. Nat Commun. 2023;14(1):5452. Published 2023 Sep 6. doi:10.1038/s41467-023-41109-9
[7] Maeda M, Murata F, Fukuda H. Effect of COVID-19 vaccination on household transmission of SARS-CoV-2 in the Omicron era: The Vaccine Effectiveness, Networking, and Universal Safety (VENUS) study. Int J Infect Dis. 2023;134:200-206. doi:10.1016/j.ijid.2023.06.017

3. Adverse event registration

The 14-day claim about adverse events, which was repeated at your press conference of 21 November 2023 and subsequently circulated on social media, is simply false. It would be in the public interest to retract this claim, as it could undermine trust in medicines and have serious implications for public health.

To be clear, regulators do not exclude reports of side effects if they occur within 14 days of vaccination. When monitoring vaccine safety, EMA and EU Member States consider all reports of suspected side effects following vaccination, regardless of how much or little time has passed from the moment the person received the vaccine to the time the suspected side effect occurred.

You can find information on how we assess safety of the vaccines on the 'Safety of COVID-19 vaccines' page on our website. You can also find further information on safety assessments on the webpages for each individual COVID-19 vaccine.

You ask whether there is a difference between the information on side effects available to the public and the information available to EMA and the companies. Data on all spontaneous reports of suspected side effects from the EudraVigilance database are available to the general public. In order to protect patient confidentiality, information for the public is partially redacted. Regulators also have access to data from non-spontaneous reports, such as reports from clinical trials and post-marketing studies, which are not always accessible to the public.

With respect to the use of vaccines in young people, it is important to note that severe COVID-19 as well as long-term effects of COVID-19 can occur in all age groups. National authorities will continue monitoring the epidemiological situation in their countries and make recommendations accordingly.

4. Batch dependent safety

In the previous reply, we described how EMA addressed quality issues during the evaluation of Comirnaty.

You cite a letter to an editor of a journal reporting preliminary data on batch-dependent safety of Comirnaty in Denmark. There are several reasons why the number of reports of suspected side effects differ by batch. Variability in reporting practices and use may result in an uneven representation of adverse events in spontaneous reporting systems. For example, different batches may be used in different demographic groups and at different stages of the pandemic. In addition, awareness of particular side effects and reporting behaviour also change over time. To date, routine surveillance has not detected a quality concern affecting the safety of specific batches.

To your question about verifying the quality of different batches, we would like to highlight that Official Medicines Control Laboratories (OMCLs) in the EU Member States check data on the quality of all batches of COVID-19 vaccines before they are released for use in the EU. Only batches that comply with EMA's approved quality specifications can be used in the EU.

You would like us to send data on 'all cause mortality related to the batches used in the EU for the last two years'. EMA staff will work on this request in accordance with our access-to-documents policy and will be contacting you separately. Please note that the information we collect in EudraVigilance concerns spontaneous reports from patients and healthcare professionals of medical events that occurred after vaccination. These events are not necessarily caused by vaccination. Some may be due to pre-existing illness or linked to causes that took effect in the same period of time. Furthermore such events can occur in both vaccinated and unvaccinated people, and only a thorough analysis can show causality.

We would also like to caution that claiming that certain batches are defective solely on the basis of the requested data would be a misuse of the data. See our comment above about the variability of reporting data for batches.

I understand you would like to request the results of investigations into the quality of all the batches used so far in the EU. EMA does not have these data, as results of such investigations are held by the OMCLs in EU Member States. As stated above, all batches released must comply with registered specifications for OMCLs to permit their release.

You also asked about the effects of mRNA COVID-19 vaccines on 'the human intestinal bacteria, the microbiome, and the risk of changes in their DNA as a result of (parts of) the content of the vaccines'. All known side effects of the vaccines are described in the summaries of product characteristics (SmPC). While gastrointestinal events are listed in the SmPCs, an effect on intestinal bacteria has not been established.

EMA will continue monitoring the safety of the vaccines and provide the public with any new information that becomes available.

5. Gene therapy

You raise concerns about what constitutes a gene therapy. In our previous reply we clarified that COVID-19 vaccines are not gene therapies under EU legislation. Part IV of the Annex to Directive 2001/83/EC and the Commission Directive 2009/120/EC are clear on this matter. It is important to note that mRNA COVID-19 vaccines do not contain genes as their active substance and, unlike gene therapies, vaccines are not used with the aim of restoring, correcting or modifying human genes.

6. Efficacy

You again raise questions about the efficacy of the COVID-19 vaccines. You also quote our previous letter in which we mentioned that efficacy wanes over time and that repeated exposure to SARS-CoV-2 could increase the chance of infection even in vaccinated people.

EMA has always been transparent about the efficacy data for COVID-19 vaccines, including uncertainties about the duration of protection and efficacy as SARS-CoV-2 evolves. We also continue to stress that COVID-19 vaccines are effective at protecting against COVID-19.

You ask us to clarify 'the time during which the vaccine is effective?' Please note that this will depend on factors such as how quickly the virus is evolving and which strains are circulating. Adapted vaccines are expected to help maintain optimal protection against COVID-19 caused by circulating strains.

To your comments about the mechanism of action, prior exposure to the spike protein following vaccination helps trigger an immune response against SARS-CoV-2, which contains the spike protein. The vaccines elicit both neutralizing antibody and cellular immune responses to the spike antigen, which contributes to protection against COVID-19.

You also ask how we 'scientifically weigh the benefits of vaccination over natural immunity'. By natural immunity, we understand you mean immunity gained after having SARS-CoV-2 infection. It is important to note that SARS-CoV-2 infection comes with the risk of severe disease and long-term effects of COVID-19 (long COVID). As of 6 December 2023, over 6.9 million COVID-19 deaths worldwide had been reported to the World Health Organization (WHO), and true mortality figures could be much higher.[8]

[8] https://ourworldindata.org/excess-mortality-covid#estimated-excess-mortality-from-the-economist

Today, most people in the EU have been vaccinated or have had COVID-19 and are therefore likely to have some immunity. However, despite past infection or vaccination, repeat infections do occur as new strains emerge and immunity wanes. With the COVID-19 vaccines currently available, national authorities can make recommendations to protect the public, including vulnerable people, taking into account the epidemiological situation in their countries.

You also request documents on the efficacy of batches used over the last 12 months. Please note that efficacy studies are not carried out separately for individual batches of vaccines. Data supporting the use of adapted Comirnaty vaccines, which have been used over the past 12 months, are available in the assessment reports on our website.[9,10, 11, 12, 13] Further data on the adapted vaccines are expected from ongoing clinical studies. As noted above, OMCLs in EU Member States check data on the quality of each batch before they are released in the EU.

Finally, we would like to reiterate that mRNA COVID-19 vaccines are effective at protecting against COVID-19. Their safety is well established and the benefits of these vaccines outweigh the risks. We maintain that denying EU citizens access to these vaccines would not be in the interest of public health.

I hope this reply addresses the issues you raise. We will be publishing it on our website.

Yours sincerely,

[redacted]

Emer Cooke
Executive Director

[9] https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-005735-ii-0140-epar-assessment-report-variation_en.pdf
[10] https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-005735-ii-0143-epar-assessment-report-variation_en.pdf
[11] https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-005735-ii-0177-g-epar-assessment-report-variation_en.pdf
[12] https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-005735-ii-0183-epar-assessment-report-variation_en.pdf
[13] https://www.ema.europa.eu/en/documents/variation-report/comirnaty-h-c-005735-x-0176-epar-assessment-report-extension_en.pdf