Medicines & Healthcare products Regulatory Agency

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[redacted]

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FOI 23/159

Dear [redacted]

Thank you for your email.

Please find below answers to the questions you have raised.

1a) Is the MHRA maintaining a database of research that has highlighted potential vaccine safety issues? If you do have such a database, can you please share it with me.

b) Has the MHRA seen the research below or any other research that highlights potential vaccine dangers?
Notes: A number of studies have highlighted potential vaccine safety issues:
e.g. here, here, here and here.

The MHRA does not hold a database of research on COVID-19 vaccines.

However, a wide range of information sources are used to monitor the safety of the COVID-19 vaccines. These include monitoring reports of suspected adverse reactions received through the Yellow Card scheme. We supplement this form of safety monitoring with other epidemiology studies including analysis of data on national vaccine usage, anonymised GP-based electronic healthcare records and other healthcare data to proactively monitor safety. We also take into account the international experience based on data from other countries using the same vaccines. Data from the companies, published literature and unpublished studies are also considered.

2a) Is the MHRA maintaining a database of people in the UK who have suffered health problems after being vaccinated? If you do have such a database, can you please share it with me, with personal details anonymised.

b) Is the MHRA in contact with individuals who have suffered health problems after being vaccinated, to give them support and monitor the progression of their health issues?

The MHRA does not hold a database of people in the UK who have suffered health problems after being vaccinated.

However, we hold a database of reports of suspected adverse reactions (Yellow Card | Making medicines and medical devices safer (mhra.gov.uk). The Yellow Card scheme is a mechanism by which anybody can voluntarily report any *suspected* adverse reactions or side effects to the vaccine. It is very important to note that a Yellow Card report does not necessarily mean the vaccine caused that reaction or event. We ask for any suspicions to be reported, even if the reporter isn't sure if it was caused by the vaccine. Reports to the scheme are known as suspected adverse drug reactions (ADRs).

You can see what types of suspected ADRs are being reported to the Yellow Card scheme as the MHRA publishes this information in the form of Interactive Drug Analysis Profiles (iDAPs). Each iDAP contains a complete listing of all spontaneous suspected adverse drug reactions, or suspected side effects, that have been reported with a particular drug substance or COVID-19 vaccine through the Yellow Card scheme.

The information published does not represent an overview of the potential side effects associated with the vaccines. A list of the recognised adverse effects of the COVID-19 vaccines is provided in the information for healthcare professionals and the recipient information. Conclusions on the safety and risks of the vaccines cannot be made on the data shown in the reports alone.

The MHRA is not in a position to provide individual advice concerning suspected adverse reactions.

3a) Has the MHRA conducted any clinical research (not statistical) to confirm how many adverse effects reported to the Yellow Card scheme since December 2020 were caused by the vaccines and not just incidental?
b) Can you please share all the research from the MHRA's investigations into these vaccine safety issues/adverse effects?
(E.g. the UKHSA has a research portal where I can access all UKHSA-funded research)

The MHRA has not conducted any clinical research to confirm how many adverse effects reported to the Yellow Card scheme since December 2020 were caused by the vaccines.

It is important to note that reporters are asked to submit Yellow Card reports even if they only have a suspicion that the vaccine may have caused the adverse reaction. The existence of an adverse reaction report does not necessarily mean that the vaccine has caused the reaction. Many factors have to be considered when assessing whether a vaccine has caused a reported adverse reaction. When monitoring the safety of medicines and vaccines, MHRA staff carry out careful analysis of these factors. However, we have not conducted clinical research on how many Yellow Card reports had a confirmed causal relationship with the vaccine.

Information on safety investigations carried out by the MHRA on these products, including the detection of rare adverse reactions are available in the published summaries of Yellow Card reporting for the primary and booster vaccination campaigns up to the end of August 2022 and the 2022 autumn booster campaign: Coronavirus (COVID-19) vaccines adverse reactions - GOV.UK (www.gov.uk).

4a) Can you explain how the MHRA reviews post-vaccination fatalities?
b) Can you share all these reviews of post-vaccination fatalities since January 2021?
Notes: In this document, the MHRA says it undertakes a thorough review of reports with a fatal outcome after vaccination.

The MHRA takes all reports with a fatal outcome in patients who have received a COVID-19 vaccine very seriously and every report with a fatal outcome is reviewed carefully. All reports with a fatal outcome regardless of the time period between receiving the suspect vaccine and the reported death are reviewed. All available information is assessed to consider whether the vaccine may have caused the reported death. Cumulatively, the Yellow Card data is thoroughly analysed for patterns or evidence which might suggest a causal link between the vaccination and the reported death alongside data available from international sources. This is further considered by the Commission on Human Medicines and its Expert Advisory Groups.

Summaries of Yellow Card reporting, including reviews of reports with a fatal outcome, are available for the primary and booster vaccination campaigns up to the end of August 2022 (ARCHIVED – Coronavirus vaccine – summary of Yellow Card reporting – GOV.UK (www.gov.uk)) and the 2022 autumn booster campaign (Coronavirus vaccine - summary of Yellow Card reporting - GOV.UK (www.gov.uk).

The MHRA continues to carefully review and monitor all reports submitted to us including those that cite a fatal outcome following COVID-19 vaccination.

5a) Does the MHRA believe single studies that have not yet been independently replicated can be relied on to determine vaccine safety and efficacy?
Notes: The clinical trials conducted by Pfizer, AstraZeneca, Moderna, Johnson&Johnson, Novavax, and Valneva to my knowledge, are single studies that have not yet been replicated.
b) Does the MHRA believe observational studies (not randomised and controlled) can be relied on to determine vaccine safety and efficacy?
Notes: In the Yellow Card summary for December 2022, three observational studies are cited as evidence for the safety of the vaccines in pregnancy (footnotes 4,5,6).
c) These studies only consider the impact of vaccination on miscarriage, stillbirth, preterm birth. Can you share the evidence that confirms these vaccines won't cause any other health issues over a number of years in children born to vaccinated mothers? The placenta theory is often cited as an answer to this question, but can the MHRA confirm that this theory won't be proven wrong in the coming years?

All the COVID-19 vaccines used in the UK vaccination programme were authorised following a rigorous review by the MHRA and the Government's independent advisory body, the Commission on Human Medicines (CHM), of their safety, quality and effectiveness. In each

case, the MHRA concluded that the COVID-19 vaccines were safe and effective and that the benefits outweighed any risk.

No medicine or vaccine is completely risk-free and hence the MHRA has continually monitored the safety of the COVID 19 vaccines through a comprehensive COVID-19 Vaccine Surveillance Strategy. This monitoring strategy is proactive and based on a wide range of information sources, with a dedicated team of scientists continually reviewing information to look for safety issues or any unexpected, rare events.

Observational studies are one form of evidence which MHRA considers in the assessment of a safety topic, however, other types of information are considered to give an overall position on the likelihood of a link between a medicine and a safety concern. Randomised controlled trials are not always feasible to investigate all safety topics.

Should a new safety issue be confirmed we will continue to act promptly to inform patients and healthcare professionals and take appropriate steps to mitigate any identified risk and protect public health.

6a) Can you please give me a full list of all the types of clinical trial documents that were submitted by Pfizer, AstraZeneca, Moderna, Novartis, Johnson&Johnson, and Valenva to the MHRA for review for the COVID vaccines they produced?
Notes: Namely: case report forms, clinical study reports, certificate of analysis, protocol, statistical analysis plan, informed consent form, serious adverse event narratives, electronic individual participant data, investigational medicinal product dossier, investigator's brochure. I can see that the MHRA has published the Public Assessment Report for these vaccines. But I can't see any other data.
b) Of these documents (or any others not named here) which ones were reviewed by the MHRA before giving approval to these vaccines?
c) Can you tell me when all these documents will be published online by the MHRA?

The clinical data for all the authorised vaccines have been published by the European Medicines Agency (EMA). A link to their clinical repository is provided below:

https://clinicaldata.ema.europa.eu/web/cdp/home

As these data are already published, the MHRA does not have any plans to publish these on-line.

Schedule 3 Part 2 of The Medicines for Human Use (Clinical Trials) Regulations 2004 includes a list of the particulars and documents that must accompany a request for authorisation of a clinical trial to the licensing authority. All of these documents are thoroughly reviewed during MHRA assessment.

Prior to authorisation for national COVID-19 vaccine applications, all of the relevant documents associated with the Common Technical Document (CTD)' submitted by the companies were assessed by the MHRA. Further information about the CTD can be found on the EMA website at Marketing authorisation guidance documents | European Medicines Agency (europa.eu).

Some authorisations for COVID-19 vaccines were authorised via the European Commission (EC) Decision Reliance Route. This is when the marketing authorisation application made by the company references the decision made by the EMA's Committee for Medicinal Products for Human Use (CHMP). In such cases, the MHRA considers the application together with due consideration of the EC decision, before making an independent decision on the quality, safety and effectiveness of the vaccine.

7a) Can you confirm when Phase 4 trials for these six vaccines concluded/are due to conclude?
b) Can you share any documents for the trials that have concluded.

Plans for post authorisation studies for COVID-19 vaccines including timelines for completion are included in the Risk Management Plans (RMPs) for COVID-19 vaccines. These RMPs are available on the EMA website as part of the European Public Assessment Reports (EPARs) for these vaccines at the links below:

https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty
https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria
https://www.ema.europa.eu/en/medicines/human/EPAR/spikevax
https://www.ema.europa.eu/en/medicines/human/EPAR/nuvaxovid
https://www.ema.europa.eu/en/medicines/human/EPAR/jcovden-previously-covid-19-vaccine-janssen
https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-inactivated-adjuvanted-valneva

You may be interested in the World Health Organisation (WHO) COVID-19 vaccine tracker and landscape which provides information on the development of COVID-19 vaccine candidates including Phase 4 trials: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.

You can also search for COVID-19 vaccine studies on the NHS Health Research Authority website (https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/), the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/) and the US clinical trials database (https://clinicaltrials.gov/).

We confirm that we hold the final study report for D8111R00007 (RAVEN), a Real-world effectiveness study of the Oxford/AstraZeneca COVID-19 vaccine in England (fulfilment of Category 3 RMP commitment) related to the clinical trial entry below:
https://clinicaltrials.gov/ct2/show/NCT05047822

However, this information is exempt under Section 22 of the FOIA. We expect that these data will be published on the EMA clinical data repository under the vaccine name Vaxzevria, in line with the EMA's publication scheme. In terms of the public interest, we do not perceive that there is a clear basis to release these data ahead of the EMA's formal publication. It should be noted that we believe it is likely that these data will also be published in online journals such as the New England Journal of Medicine, and the MHRA could be placed at risk in relation to the duty of confidence were we to release these data ahead of the relevant publisher/journal(s). We appreciate that the new effectiveness data

could be of interest to the public once assessed. If any key insights are drawn from these data updates, these will be published in the SmPC and if applicable/necessary, through changes to the recommendations in the patient information leaflet (PIL). Any updates necessary will occur rapidly so that healthcare providers and patients will be swiftly informed of any new information of significance, for example, the inclusion of new information and guidance relating to matters of safety, or efficacy.

We consider exemption of documentation under Section 22 in this case is:

- sensible;
- in line with accepted practices;
- fair to all concerned

If you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within two months of the date you receive this response and addressed to: info@mhra.gov.uk

Please remember to quote the reference number above in any future communications. If you were to remain dissatisfied with the outcome of the internal review, you would have the right to apply directly to the Information Commissioner for a decision.

Please bear in mind that the Information Commissioner will not normally review our handling of your request unless you have first contacted us to conduct an internal review.

The Information Commissioner can be contacted at:
Information Commissioner's Office
Wycliffe House
Water Lane
Wilmslow
Cheshire
SK9 5AF

Yours sincerely,