Medicines & Healthcare products
Regulatory Agency

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United Kingdom
gov.uk/mhra

[redacted]

29 January 2023

Dear [redacted],

Thank you for your request for information dated 1 January 2024, we have copied your list of questions below and placed our responses beneath each question.

1. Please provide the conditions that are required to be met by the licensing authority that would signal a pause and reappraisal of the associated Covid-19 Messenger RNA vaccines approved under Emergency Use Authorisation (EUA).

Our response:
We have interpreted your mention of 'Emergency Use Authorisation (EUA)', a term used by the FDA, to relate to the MHRA Temporary Authorisation of the COVID-19 mRNA vaccines under Regulation 174.

The meaning we have drawn from the phrasing of your question, is that this appears to relate to factors which would lead to an overall decision on to suspend an R.174 Authorisation. Many different factors are considered when assessing the benefit-risk balance of a medicinal product and including the number of people who have received the product, the seriousness of the disease being treated, the availability and effectiveness of other treatments, the seriousness and frequency of the adverse reactions(s) and the indication and efficacy of the product. The MHRA's continuous evaluation of the safety of the COVID--19 vaccines authorised in the UK supports our position that the benefits continue to outweigh the known risks for the vast majority of people.
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Please note, no batches of Moderna COVID-19 vaccine (mRNA-1273) were supplied under the Reg174 approval.

There are lists of conditions published online for the R.174 Pfizer/BioNTech vaccine, but these conditions relate to manufacture & supply of this vaccine.

You may also be interested in the below:
Regulations 174A and 247A: one-year review - GOV.UK (www.gov.uk)

Public assessment reports for the regulation 174.
Public Assessment Report (publishing.service.gov.uk) - Pfizer/BioNTech vaccine

Please also note, the R.174 temporary authorisations for the mRNA vaccines have since been superseded by the marketing authorisations.

- A marketing authorisation was granted for the Pfizer/BioNTech vaccine (Comirnaty) following a European Commission (EC) decision on 21 December 2020 (PLGB 53632/0002).
- A marketing authorisation was granted for the Moderna vaccine on 31 March 2021 following an EC Reliance Procedure (PLGB 53720/0002)

Details of these authorisations are on the EMA website.

Spikevax (previously COVID-19 Vaccine Moderna) | European Medicines Agency (europa.eu)
Comirnaty | European Medicines Agency (europa.eu)

> 2. Please provide copies of MHRAs Safety Audits since the rollout of Covid-19 Messenger RNA Vaccines approved under Emergency Use Authorisation (EUA).

Our response:
This information is not held. The MHRA has a statutory obligation under the Human Medicines Regulations to audit its pharmacovigilance system every two years. During COVID-19, some elements of the audit programme were rescheduled using a controlled approach to ensure that resources were fully focused on signal detection and assessment. The systems used for signal detection have been subject to many previous internal and external audits with no significant findings and the approach was aligned to that taken by other international regulators.

> 3.Please provide your updated Age Stratification Risk/Benefit Profile of Covid-19 Messenger RNA Vaccines approved under Emergency Use Authorisation (EUA).

Our response:
This information is not held.

The benefit-risk for the original authorisation of the vaccines under Regulation 174 is available in the Public Assessment Reports that were published as noted as above. Our ongoing review supports the position that benefits outweigh known risks for all age groups in which vaccines are authorised.

> 4. Please provide your risk assessment of widely applied vaccination during a respiratory virus pandemic using an imperfect vaccine that does not disrupt transmission or infection.

Our response:

We hold no information specifically for a “widely applied vaccination during a respiratory virus pandemic using an imperfect vaccine that does not disrupt transmission or infection” and it is not a regulatory requirement to do so.

We have provided our full assessment of all authorised vaccines, as have the European Medicines Agency, who have also published the clinical data submitted in their clinical repository.

Home - Clinical Data Publication - clinicaldata.ema.europa.eu

5. Please provide a copy of the Genotoxicity studies performed on the mRNA Covid-19 vaccines before their approval and rollout.

Our response:
COVID-19 Vaccine Moderna, 0.20 mg/mL dispersion for injection
Genotoxicity studies were *not performed on finished product COVID-19 Vaccine Moderna, 0.20 mg/mL dispersion for injection in terms of the final product. However, please note preclinical testing on some components of the vaccine were undertaken. A separate request could be made for this information if it would be of interest.*

Pfizer/BioNTech vaccine
Please see page 20 of the below-linked PAR for the Pfizer vaccine. It states that “no genotoxicity studies are planned for BNT162b2, as the components of all vaccine constructs are lipids and RNA that are not expected to have genotoxic potential (WHO, 2005).”

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1112667/COVID-19_mRNA_Vaccine_BNT162b2__UKPAR___PFIZER_BIONTECH_ext_of_indication_11.6.2021.pdf

6. Please provide your risk assessment of frequent mRNA boosters for Covid-19 disease and adverse effects to the hosts immune system, including Endoplasmic Reticulum (ER) Stress and IGG4 Class Switching.

Our response:

If this request intends to seek one overarching report ie. one risk assessment, then one such report is not held; rather it is the case that review of ongoing safety and adverse event data takes place. Our ongoing review of the mRNA COVID-19 vaccines supports position that the benefits continue to outweigh known risks.

7. Please confirm if any of the Vaccines approved under emergency authorisation against Covid-19 disease instruct a person’s own body to repeatedly manufacture the spike protein. If so, for how long.

Our response:
While we may hold some journal articles that are freely available online in relation to the estimated persistence of the spike protein following vaccination, given the variance between individuals in terms of their own biology it is not possible for us to determine how long the

spike protein will remain in each person's body, and we do not hold information to answer this specific question.

The vaccine consists of RNA molecules contained in a carrier molecule such as liponanoparticles (LNPs). The target cells take up the RNA molecules (contained in the carrier molecule), the mRNA is translated into Spike proteins inside the cytoplasm, and then, the protein viral antigen is expressed on the cell surface. It is not expected that the delivered mRNA enters the cell nucleus or interacts with the genome. mRNA molecules are non-replicating and are only expressed transiently in cells.

> 8. Please confirm if MHRA have a Vaccine Crisis Communication Manual in the event of an untoward medical occurrence following immunization against COVID-19, and as a result could potentially create uncertainty and/or erode the public's trust in vaccines and/or vaccination and the authorities delivering them

Our response:

We note the reference to the WHO document concerning the Vaccine Crisis Communication Manual: WHO-EURO-2022-3471-43230-60590-eng.pdf which is intended for use by stakeholders in national immunisation programmes.

We do not hold the requested document. Through adherence to the Human Medicines Regulations (2012) and the guidance in the Good Vigilance Practice modules, MHRA has robust procedures in place to monitor the safety of vaccines in the post marketing period and works closely with the UK Health Security Agency to take swift action as necessary in the event of a vaccine crisis situation.

We trust that you will find these answers uesful. However, if you disagree with how we have interpreted the Freedom of Information Act 2000 in answering your request, you can ask us to review our actions and decisions by writing to: info@mhra.gov.uk, and requesting an internal review.

Please note that your internal review request must be in a recordable format (email, letter, audio tape etc.), and that you have 40 working days upon receipt of this letter to ask for a review. We aim to provide a full response to your review request within 20 working days of its receipt. Please quote the reference number above in any future communications.

If you are not content 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 online via an electronic form: https://ico.org.uk/make-a-complaint/foi-and-eir-complaints/foi-and-eir-complaints/

Or in writing to:
Information Commissioner's Office,
Wycliffe House,
Water Lane,
Wilmslow,

Cheshire,
SK9 5AF

Yours sincerely,

MHRA Customer Experience Centre
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