FOI 22/1223 Pfizer Comirnaty ALC-0315 and ALC-0159

REQUEST

22 December 2023

In light of a recent Australian FOIA request (previously redacted) made public (Non Clinical Evaluation Report - PM-2020-05461-1-2) can you provide further information on the UK authorisation of novel excipients ALC-0315 and ALC-0159 in the Pfizer mRNA Comirnaty product?

The Australian report stated that the novel excipients are not expected to be genotoxic or carcinogenic - but that the single species and low number of data were of concern but were 'adequately justified' by the Sponsor (Pfizer). What 'justification' was allowable for the same authorisation in the UK?

Neither genotoxicity nor carcinogenicity studies were performed. The components of COMIRNATY (lipids and mRNA) are not expected to have genotoxic potential - 'expected' is not a sufficient authorisation for novel excipients en-masse to the British Public - please provide UK specific data on genotoxicity and carcinogenicity.

What transfection studies (introduction of foreign DNA into cells) were completed?

Given you probably know the Comirnaty 'vaccine' transfects (gene altering) what additional regulatory authorisations concerning gene altering / genetic products were sought by MHRA or other Govt Depts in authorising this Pfizer therapy?

Knowing this transfection rate and high concentration of the product 48h post injection in female ovaries, why did you continue to authorise this product as safe for pregnant women when the sample size was so small (n=3) and the long-term detrimental effects are still unknown?

MHRA RESPONSE

20 January 2023

Dear

Thank you your email.

We are pleased to provide you with the information requested, see below.

The UK marketing authorisations for Comirnaty were done via reliance route procedures, so

MHRA's assessment decision is based on the assessment done by the EMA. Further information, including the EMA PAR for this medicinal product, is available via the below link: https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.ema.europa.eu%2Fen%2Fmedicines%2Fhuman%2FEPAR%2Fcomirnaty&data=05%7C01%7CMHRACustomerServices%40mhra.gov.uk%7C923b9efd48a448d9a0bd08dafacb42cb%7Ce527ea5c62584cd2a27f8bd237ec4c26%7C0%7C0%7C638098048150984795%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=gAEYjHnQnv1hovhOvgckhp29hFM0i9HHk5rbvd72SHM%3D&reserved=0

The original Public Assessment Report (PAR) published by the EMA provides details of the assessment of the Comirnaty vaccine, including the assessment of ALC-0315 and ALC-0159 and the assessment of genotoxicity. A link to the PAR is provided below: https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.ema.europa.eu%2Fen%2Fdocuments%2Fassessment-report%2Fcomirnaty-epar-public-assessment-report_en.pdf&data=05%7C01%7CMHRACustomerServices%40mhra.gov.uk%7C923b9efd48a448d9a0bd08dafacb42cb%7Ce527ea5c62584cd2a27f8bd237ec4c26%7C0%7C0%7C638098048150984795%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=SLrB9PzAfusVV0DzzZDAgQNhnGhnSSdb7WDoM0SnRcE%3D&reserved=0

Regarding the use of the vaccine in pregnant women, assessment of the reproductive toxicity of the Comirnaty vaccine is available in Sections 4.6 and 5.3 of the SmPC is available via the below link:

https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.gov.uk%2Fgovernment%2Fpublications%2Fregulatory-approval-of-pfizer-biontech-vaccine-for-covid-19%2Fsummary-of-product-characteristics-for-covid-19-vaccine-pfizerbiontech%23%3A~%3Atext%3DThe%2520booster%2520dose%2520of%2520Comirnaty%2Cof%2520a%2520COVID-19%2520vaccine&data=05%7C01%7CMHRACustomerServices%40mhra.gov.uk%7C923b9efd48a448d9a0bd08dafacb42cb%7Ce527ea5c62584cd2a27f8bd237ec4c26%7C0%7C0%7C638098048150984795%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=aL4yukljACV6guhyfeY5X1UJykOMMAxR2D%2BO7ZK0hcE%3D&reserved=0.

A genotoxic action requires the material to come into contact with the genetic material of a cell: however, ALC-0315 and ALC-0159 associate with the cell membrane and do not penetrate into the cells where the genomic material is in the nucleus, and thus genotoxicity studies were not required. Carcinogenicity studies are not required for products that are given over a very short period: usually, products that are given continuously for 6 months or more require carcinogenicity evaluation. These aspects were considered in the UK authorisation of this product.

The action of reverse transcriptase enzymes is specific and has likely evolved over millenia: however, the RNA in Comirnaty is novel, and its transcription into DNA considered not at all likely to occur due to a lack of reverse transcriptase enzymes with this specificity. The safety of vaccines continues to be monitored in the longer term using the Yellow Card System by which adverse events that are suspected as reactions to the vaccine can be reported.

The vaccine was initially used in the elderly, in whom use in pregnancy was not a concern. By the time it was used in younger vaccinees, there were data from studies in pregnant animals that indicated it could be used safely.

If you disagree with how we have interpreted the Freedom of Information Act 2000 with regards to your request, you can ask for the decision to be reviewed. The review will be carried out by a senior member of the Agency who was not involved with the original decision.

If you have a query about the information provided, please reply to this email.

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

MHRA Customer Service Centre

Medicines and Healthcare products Regulatory Agency
10 South Colonnade, Canary Wharf, London E14 4PU