Medicines & Healthcare products
Regulatory Agency

10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom
gov.uk/mhra

Mr N H Hunt
By email: _____

21 September 2023

Dear Mr N H Hunt

Internal review of FOI 23/510

We are writing in response to your request of 26 July 2023 for an internal review of the Medicines and Healthcare products Regulatory Agency's ('the Agency') response to your FOI request (**FOI 23/510**).

We confirm that an internal review has been conducted and hereby set out its findings.

Request history

On 13 July 2023 you made the following request for information:

> *"1. Temporary Authorisation of the Pfizer Covid vaccine on 2 December 2020 permitted public use of Batch EJ0553 based, inter alia, on the clinical trials in 2020 defined in Pfizer document C4591001. The vaccine used in the 2020 clinical trials was manufactured using 'Clinical Supply' 'Process 1'. Batch EJ0553 was manufactured in September 2020 using 'Commercial Supply' 'Process 2'.*
> ***Request 1 : please can you tell me if any human was vaccinated (in UK or elsewhere) using 'Process 2' product prior to 2 December 2020, and if so, when and where.***
>
> *2. Pfizer amended C4591001 in October 2020 to add, inter alia, at para 9.4 : "The safety and immunogenicity results for individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" and each lot of "Process 2" will be summarized descriptively. A random sample of 250 participants from those vaccinated with study intervention produced by manufacturing "Process 1" will be selected randomly for the analysis."*

Request 2 : Please can you send me a copy of Pfizer's report of this. Alternatively, if you exempt its release, tell me the Pfizer reference and date.

3. Page 69 of https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf states that "The scale of the BNT162b2 manufacturing has been increased to support future supply. BNT162b2 generated using the manufacturing process supporting an increased supply (commercial process) will be administered to approximately 250 participants 16 to 55 years of age, per lot, in the study. Data are expected in February 2021.

***Request 3 : Please can you send me a copy of Pfizer's report of this. Alternatively, if you exempt it release, tell me the Pfizer reference and date**."*

The Agency responded to your request on 26 July 2023 as follows:

Dear Mr N H Hunt,

Thank you for your email.

Please find below answers to the questions you have raised below.

"Question
1. Temporary Authorisation of the Pfizer Covid vaccine on 2 December 2020 permitted public use of Batch EJ0553 based, inter alia, on the clinical trials in 2020 defined in Pfizer document C4591001. The vaccine used in the 2020 clinical trials was manufactured using 'Clinical Supply' 'Process 1'. Batch EJ0553 was manufactured in September 2020 using 'Commercial Supply' 'Process 2'.
Request 1 : please can you tell me if any human was vaccinated (in UK or elsewhere) using 'Process 2' product prior to 2 December 2020, and if so, when and where.

Answer
The clinical data submitted for the Pfizer vaccine has been published by the EMA in their clinical repository. This includes the clinical study reports, which should contain information on the batches of vaccine that were used in each trial. Link to the EMA clinical repository is below:
https://clinicaldata.ema.europa.eu/web/cdp/home

Questions 2 & 3
2. Pfizer amended C4591001 in October 2020 to add, inter alia, at para 9.4 : "The safety and immunogenicity results for individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" and each lot of "Process 2" will be summarized descriptively. A random sample of 250 participants from those vaccinated with study intervention produced by manufacturing "Process 1" will be selected randomly for the analysis."
Request 2 : Please can you send me a copy of Pfizer's report of this. Alternatively, if you exempt its release, tell me the Pfizer reference and date.

3. Page 69 of https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf states that "The scale of the BNT162b2 manufacturing has been increased to support future supply. BNT162b2 generated using the manufacturing process supporting an increased supply (commercial process) will be administered to approximately 250 participants 16 to 55 years of age, per lot, in the study. Data are expected in February 2021.

Request 3 : Please can you send me a copy of Pfizer's report of this. Alternatively, if you exempt it release, tell me the Pfizer reference and date.

Answer
2. & 3. The clinical data submitted for the Pfizer vaccine has been published by the EMA in their clinical repository. If the report has been submitted to the EMA and MHRA, it will be available in the clinical repository. Link to the EMA clinical repository is below:
https://clinicaldata.ema.europa.eu/web/cdp/home"

On 27 July 2023, you sought a review of this response:

Thank you for your reply.

"However, this is to request an Internal Review about the handling of my FOI request for the reasons which follow.

My questions were VERY specific; namely,

a) when and where the first human was vaccinated using P2 product (Q1);

and which Pfizer report(s) relate to some VERY specific trials to compare the safety and immunogenicity of P1 and P2 production batches which were :
b) promised by Pfizer in the reference in my Q2
c) referred to by the EMA in the reference in my Q3

It is not therefore helpful, open or transparent for MHRA to reply to my very specific questions by just giving me the link to an EMA website containing hundreds of documents relating to the Pfizer Covid vaccine and say, in effect, "go and look for yourself". The answer to my questions are a crucial part of the safety audit trail underpinning Temporary Authorisation of the Pfizer Covid vaccine on 2 December 2020 ; namely, the safety evidence to bridge between the clinical trials which used Process 1 product and TA which was for a Process 2 batch. You will, therefore, know precisely which Pfizer report(s) prior to 2 December 2020 confirmed the safety and immunogencity of Process 2 product.

As it happens, prior to asking this FOI, I had already trawled the EMA database, as well as wider internet searches, looking for any Pfizer reports which answered my questions. The only report I had found which came anywhere near was Pfizer report C4591017 of a trial conducted between 15 February - 22 July 2021 to evaluate the

safety, tolerability and immunogenicity of multiple production lots on numbers of subjects not too dissimilar to those quoted in my FOI request. Unfortunately, that study post-dates MHRA's Temporary Authorisation (TA) of the Pfizer Covid vaccine on 2 December 2020. Which is why I made this FOI request.

So, this boils down to either :

- *confirm (or not) that Pfizer report C4591017 is the answer to my Questions 2&3*
- *conduct an Internal Review focussing on how you justify answering my very specific questions with a link to a website containing hundreds of Pfizer documents when you must, by dint of having granted TA for a P2 batch when clinical trials to that point used P1 product, already know the specific answers, and hence should provide them."*

Issues on review

Firstly, from the points you have raised in your request for review, whether:

- *Pfizer report C4591017 is the answer to my Questions 2&3*

Following this, the internal review then considered:

i) whether the relevant information was identified, and
ii) whether the response complied with the requirements of section 1(1)a (to confirm that the information is held) and 17(4) (to state the exemption applied and explain why it applies)

Consideration of the issues

We can confirm that the Pfizer report C4591017 is not relevant to questions 2 and 3.

i) whether the relevant information was identified

The original responses directed you to the clinical data repository hosted by the EMA. The review finds that the responses were not compliant with the Act and did not provide or address the specific information that your questions asked for.

At internal review, we hope to be able to provide direct responses and address the questions which you raise directly.

Request 1 : please can you tell me if any human was vaccinated (in UK or elsewhere) using 'Process 2' product prior to 2 December 2020, and if so, when and where.

Answer:
This information was not held at the time of your request; this should have been indicated under section 1(1)(a).

Further to this, we can advise that Pfizer/BioNTech confirmed that the first clinical batch which contained process 2 drug substance was dosed 19th October 2020 in US.

2. *Pfizer amended C4591001 in October 2020 to add, inter alia, at para 9.4 : "The safety and immunogenicity results for individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" and each lot of "Process 2" will be summarized descriptively. A random sample of 250 participants from those vaccinated with study intervention produced by manufacturing "Process 1" will be selected randomly for the analysis."*

   Request 2: Please can you send me a copy of Pfizer's report of this. Alternatively, if you exempt its release, tell me the Pfizer reference and date.

Answer:
Under section 1(1)(a), the review confirms a report specifically on analysis on the "*random sample of 250 participants vaccinated with study intervention produced by manufacturing "Process 1"*" is not held.

To provide helpful context and background, in the early stages of the pandemic, before BNT162b2 was authorised or approved, improvements were made to the manufacturing process to adjust the scalability, robustness, and productivity in preparation for large scale manufacture (Process 2); scaling of manufacturing processes is a common occurrence in the manufacture of medicines. Manufacturing steps that were not scalable were replaced with those designed to provide a similar or better impurity profile.

This "process 2 drug" substance was shown to be comparable through side-by-side comparability studies and heightened characterisation testing. The process was validated at all manufacturing sites and submitted for review and approval. Vaccines produced by both "Process 1" and "Process 2" were included in the pivotal clinical trial[1] (C4591001).

Typically, such changes can be supported by analytical data; however, due to the nascent regulatory landscape for COVID-19 vaccines, in October 2020 an exploratory objective was added in the C4591001 study to describe safety and immunogenicity of vaccines produced by manufacturing "Process 1" or "Process 2" in participants 16 to 55 years of age. This exploratory objective was removed and documented in protocol amendment 20 in September 2022 due to the extensive usage of vaccines manufactured via "Process 2". Thus, this process comparison was not conducted as part of the formal documentation within the protocol amendment.

As with all vaccines and medicines, the safety of COVID-19 vaccines is being continuously monitored. For all COVID-19 vaccines, the overwhelming majority of reports relate to injection-site reactions (sore arm for example) and generalised symptoms such as 'flu-like' illness, headache, chills, fatigue (tiredness), nausea (feeling sick), fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these happen shortly after the vaccination and are not associated with more serious or lasting illness.

Request 3: see bold italic text below.

3. Page 69 of https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf states that "The scale of the BNT162b2

[1] Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine | NEJM

manufacturing has been increased to support future supply. BNT162b2 generated using the manufacturing process supporting an increased supply (commercial process) will be administered to approximately 250 participants 16 to 55 years of age, per lot, in the study. Data are expected in February 2021.

***Please can you send me a copy of Pfizer's report of this. Alternatively, if you exempt it release, tell me the Pfizer reference and date**.*

This request appears to also ask for a Pfizer study in respect of the 250 participants and appears to be a duplicated question, asking for the same information as was sought in question 2. As described above for question 2, a report on the 250 participants is not held. Our original response should have advised this. Please note, the route of authorisation followed for this vaccine was the European Commission Decision Reliance Procedure.

3. Conclusion and recommendations

This internal review has identified that our original response to your request did not meet the requirements of the FOIA, and we should have confirmed whether information that is subject of an FOI request is held or is not held. We have used the opportunity of this internal review to directly answer each question to confirm that the information is not held, and provided further assistance for questions 1, 2 and 3.

To make an additional observation on the original response, this did not include any exemptions (Sections) of the FOIA, but the responses did refer to information in the public domain. Under best practice, responses should first confirm if the information is held or not held. In cases where the relevant information is held, but the same information is also published by ‘another person’ the Section 21 exemption should be considered and where appropriate to do so, engaged.

We hope that this review is useful for you and has clarified the position on the information you requested. If you remain dissatisfied, you may ask the Information Commissioner (ICO) to make a decision on whether or not we have interpreted the FOIA correctly in dealing with the request and subsequent internal review. The ICO’s address is:

The Information Commissioner’s Office
Wycliffe House
Water Lane
Wilmslow
Cheshire
SK9 5AF

Yours sincerely

MHRA Customer Experience Centre
Communications and engagement team
Medicines and Healthcare products Regulatory Agency
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