Medicines & Healthcare products Regulatory Agency

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London
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gov.uk/mhra

[redacted]

20 February 2024

Dear [redacted]

FOI 24/075 - FOI request regarding subject 10841470 male 65, in the Pfizer trial.

Thank you for your request for information, to ensure the background information to your request is not lost, this response begins with your request history.

Request history

On 12 December 2023, you made the below request for information (FOI 23/972).

> *"I would be grateful if you would send me all of the information you hold on the following Pfizer trial participant. He is the placebo group participant who died on 11.1.2021 after having one dose of Moderna COVID-19 vaccine on 23.12.2020, via his employer.*
> *Please include any tables that his death is recorded in. His death was one of the 38 deaths that occurred between dose 1 and the data cutoff of 13.3.2021 and one of the 29 deaths that occurred during the blinded, placebo-controlled part of the study, so please include any tables relating to these deaths.*
>
> *> Participant.....10841470 male 65*
> *>*
> *> Study sponsor.....BioNTech*
> *> Study conducted by.....Pfizer*
> *> Study intervention number.....PF07302048*
> *> Study intervention name.....RNA-Based COVID-19 Vaccine Protocol number.....C4591001*

> Phase.....1/2/3
> Short title:
> A Phase 1/2/3 Study to Evaluate the Safety, Tolerability and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals."

On 15 Jan 2024, we replied with a refusal under Section 12 of FOIA

"We wish to inform you that we want to be as open as possible in answering requests or information. We can confirm that MHRA does hold some information within scope of your request. However, your request is very broad primarily due to the terminology used 'all information' ... about a specific trial participant. After preliminary searches we have established that gathering all the information we hold on this participant, as per the requirements of the FOIA, would exceed the limits under Section 12 of the FOIA. We have reached this conclusion because:

- The term 'all' would require us to conduct an expansive search through the clinical study report, associated annexes, possibly assessment reports, and also any other material where this participant may be cross-referred to.
  Two members staff have spent significant amounts of time locating information in preliminary searches.

- While the participants death will be recorded in tables in the clinical study report this will be not be linked with the subject number-which in this document will appear on a separate page. Therefore, the cause/s of death and other details would need to be manually cross-referenced to other relevant tables in the clinical study report.

- Clinical trial information has been submitted in tranches throughout the lifecycle of the vaccine.

Section 12(1) of the FOIA allows MHRA to refuse a request for information if we estimate that the cost of complying with the request would exceed the appropriate fees limit for determining whether we hold the information, and in locating, retrieving and extracting the information. Whilst we have located some of information within scope of your request, it has become clear that the cost limit would be exceeded by a complete search as set out in section 12(1) of the FOIA and we have therefore ceased any further searches. Section 16 of the Freedom of Information Act requires MHRA to provide advice and assistance to the requestor, and this is provided below.

Advice and assistance
If you wish to submit a narrowed request, we would suggest requesting the

participant's narrative of death which in the adjacent pages is accompanied by tables of the participants biometric information. However, we would like to advise that FOI is a disclosure to the world and on receipt of a narrowed request, we will need to consider whether any exemptions under the FOI apply - we'd therefore like to make you aware that health information relating to deceased individuals may be covered by section 41 (information provided in confidence).

If you wish, it may be an option for you to approach the Marketing Authorisation Holder (MAH) with your enquiry directly: Contact Information for Healthcare Professionals | Pfizer Medical Information – UK"

On 23 January 2024 you replied with following request:

"Many thanks for your reply.
I much appreciate that you have explained the issues.
In view of what you have said, could you please send me the following:

1. *The subjects narrative report.*

2. *Any tables you have tabulating deaths in the Pfizer trial similar to the two I enclose below (first page of each enclosed) complete with footnotes. The first is already available on the FDA website in a BLA Clinical Review Memorandum and the second is now available to the public at the US Public Health and Medical Practitioners for Transparency website after the intervention of a federal judge. The FDA's version of his narrative record is also available unredacted at that website (copy below). You do not need to add any participant number if it is not already in the table.*

3. *The results of his 2 antibody tests, blood was taken for immunogenicity at visit 1 on 30.9.20 and visit 3 on 18.11.20."*

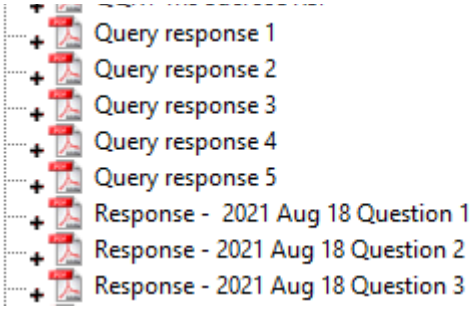
Screenshots of similar information available on the FDA website and another public website were also provided with your request. In order to reduce the length of this letter, your screenshots are included in the annex I of this letter.

Our response

Regarding your request MHRA estimate that compliance with this request would exceed the appropriate limit under Section 12 of the Freedom of Information (FOI) Act 2000, which is set at 24 working hours per request. Public authorities are not obliged to work past the appropriate limit under Section 12(1) of the FOI Act 2000 and we are, therefore, unfortunately refusing your request.

Explanation of steps needed to identify, locate, extract and retrieve the information:

- In terms of the 2nd question the phrasing was "Any tables you have tabulating deaths in the Pfizer trial similar to the two I enclose below (first page of each enclosed) complete with footnotes." While we appreciate the screenshots were intended to be helpful to direct our search. The first appears to be the FDA's assessment of deaths associated with cardiovascular disease. I've identified the screenshot as originating from the following document: https://www.fda.gov/media/152256/download. A document which relates to a Biologics License Application (BLA) Clinical Review Memorandum. The language of 'similar to' is quite non-specific we would need to check the iterative versions of internal assessment reports to ascertain if 'similar' information is held. Please also note, the MHRA produces public assessment reports, based on MHRA's assessor's reports which are available online, for example: https://assets.publishing.service.gov.uk/media/63529601e90e07768265c115/COVID-19_mRNA_Vaccine_BNT162b2__UKPAR___PFIZER_BIONTECH_ext_of_indication_11.6.2021.pdf .
- The second screenshot appears to relate to documentation submitted to the FDA by Pfizer/BioNtech. It is likely that we hold the same specific table/document, however, once again from the wording/phrasing of 'similar to', it is unclear what specifically you are requesting; the same table, or similar tables and what form these might take, for example, deaths occurring earlier or later within the different clinical trial data cut-off points? Therefore, we would need to check all sequences with clinical data to check if similar tables are included. A clinical assessor has identified ~280 sequences (indexes of files) that are likely to contain clinical data. A key point is that while we can check a date when a sequence of data was submitted to MHRA, it is more difficult to establish the dates referred to in the documents provided in a specific sequence. A further point is that while we can search for a specific subject/participant within a document, we do *not* currently have the facility to reliably search for the same across multiple documents in a sequence/s, this significantly increases the amount of time required to conduct searches, as each file needs to be opened.
    - Due to the non-specific wording of part 2 of your request, to avoid inadvertently restricting your request's scope. We interpret 'similar to', to take on a broad meaning, one that would include tables related to this participant, their data and tables related to deaths occurring in the trial C4591001.
- Please note, responses can be received by MHRA from the company, and these are stored in a different module of the dossier. A response or set of responses could include tables of deaths / death listings, and comments on deaths. Therefore, we would need to check at least two locations in the above-mentioned sequences. A later response may cross-reference earlier data, so it is difficult to arrive at time window of sequences to narrow the search to suggest a refinement in this manner. Please also note, responses files are often not titled based on their content. Instead, these are usually numbered and so locating which responses may contain tables on deaths (if any) will be a highly time-consuming manual cross-checking exercise. A screen-shot example is provided below to illustrate this:



- While FOI is motive blind, sharing more details about the intention of your request may help us to identify the specific information sought. We are also unclear why the same narrative document as held by the FDA has been requested. However, we can provide this information, and this will be discussed further in our advice and assistance to you.

Section 16 of FOI Act outlines responsibilities to provide reasonable advice and assistance to people who propose to make, or have made, requests for information. In order to assist you, we would like to mention that the EMA host clinical data for the Pfizer/BioNTech Vaccine, please note the current authorisation for this vaccine in Great Britain was granted under the Reliance procedure. While we fully expect the clinical data hosted on this site to be identical to that held by MHRA for the trial, we could only establish this by conducting a page-by-page verification. In terms of part 3. of your request, we are unsure if you are requesting a binary C-19 antibody test result for this participant e.g. positive Y/N, or details of any test antibody test results for this participant that may have occurred throughout the trial. I also note that the published study for this trial mentions "(SARS-CoV-2 N-binding antibody) will be reported later", this means we may hold more detailed information on antibody testing results. Nonetheless,

In terms of a refined request, we would suggest proceeding with part 1. of your request only:

1. The subjects narrative report."

We hold the text narrative and three introductory pages of tables concerning demographic details and medical history for the participant. Please note, while we expect to be able to release this information, it is still possible that some of these details will be exempt under a certain section or sections of the FOIA.

We trust that you will find this guidance of use. 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
Communications and engagement team
Medicines and Healthcare products Regulatory Agency
10 South Colonnade, Canary Wharf, London E14 4PU
Telephone 020 3080 6000

Annex I - screenshots provided with request 24/075.

protocol-specified efficacy analyses of severe COVID-19 cases. Abbreviated narratives are provided for those participants who died from COVID-19 in Appendix C.

Cardiac conditions were reported as the cause of death for 9 participants (cardiac arrest [7], congestive heart failure [1] and cardiovascular disease [1] who had received at least one dose of BNT162b2. The time from the last dose of BNT-162b2 to a cardiac- related death was 25-128 days. The event occurring 25 days from Dose 1 BNT162b2 occurred in a subject who had previously received two doses of placebo and was classified as cardiopulmonary arrest secondary to aortic stenosis. In the placebo group there were 5 cardiac related deaths (2 myocardial infarction, 1 aortic rupture, 2 cardiac arrest) occurring 15-81 days following study intervention (placebo). This excludes deaths due to COVID-19 which may have included cardiac-related presentations as part of the clinical course.

> *Reviewer Comment:* Based on clinical review of the individual cases, the lack of a clear temporal association to vaccination, the presence of confounding factors (e.g., pre-existing comorbidities) and the small number of cases, FDA assessed these deaths as unlikely to be related to vaccination.

Table 32. Deaths from Dose 1 to Data Cutoff of March 13, 2021, Phase 2/3 Participants 16 Years of Age and Older, Safety Population

Vaccines Received	Age/Sex	Number of Doses	Time Since Last Dose (days)	Cause of Death
BNT162b2	56/F	2	62	Cardiac arrest
BNT162b2	54/M	2	87	Congestive heart failure
BNT162b2	64/M	2	90	MVA
BNT162b2	84/M	2	70	Cardiovascular disease
BNT162b2	77/M	2	120	Emphysematous cholecystitis and sepsis
BNT162b2	82/M	2	142	Metastatic pancreatic cancer
BNT162b2	63/F	2	69	COPD
BNT162b2	86/F	2	97	Septic shock due to bowel obstruction
BNT162b2	63/F	2	41	Sudden cardiac death
BNT162b2	58/F	2	72	Cardiac arrest
BNT162b2	51/M	2	112	Metastatic lung cancer
BNT162b2	53/M	2	85	Cardiopulmonary arrest
BNT162b2	78/F	2	128	Cardiac arrest
BNT162b2	76/M	2	30	Cardiac arrest
BNT162b2	58/M	2	116	Cardiac arrest following seizure &
BNT162b2	72/M	1	35	Shigella sepsis
BNT162b2	62/F	2	73	MVA^
BNT162b2	60/M	1	3	"Atherosclerosis" (Found dead at home)
BNT162b2	80/M	2	109	COVID pneumonia*
Placebo/ BNT162b2	84/M	2/ 1	25	Cardiopulmonary arrest secondary aortic stenosis
Placebo/ BNT162b2	67/M	2/ 1	4	Suicide
Placebo	67/M	2	86	Metastatic biliary cancer

16.2.7.7 Listing of Deaths – All Subjects ≥16 Years of Age

Age Group (Years)	Subject	Dose No.	Rel Day[a]	Sex	Date of Death	Age at Death (Years)	Primary Cause of Death	Secondary Cause(s) of Death
16-55	C4591001 1021 10211127∞	2	88	M	19DEC2020	54	Cardiac failure congestive	
	C4591001 1081 10811194	2	37	F	04NOV2020	51	Myocardial infarction	
	C4591001 1120 11201266∞	2	113	M	19JAN2021	51	Lung cancer metastatic	
	C4591001 1127 11271112∞	2	86	M	04DEC2020	53	Cardio-respiratory arrest	
	C4591001 1152 11521085	1	8	F	26AUG2020	42	Death	
	C4591001 1156 11561124	2	32	M	02NOV2020	53	Overdose	
	C4591001 1229 12291083†	2	76	F	05JAN2021	56	COVID-19 pneumonia	
	C4591001 1231 12314987	2	82	M	06DEC2020	47	Cardio-respiratory arrest	
>55	C4591001 1007 10071101∞	2	63	F	21OCT2020	56	Cardiac arrest	
	C4591001 1019 10191146	2	87	M	17DEC2020	67	Metastases to liver	Biliary cancer metastatic
	C4591001 1027 10271191#	2	135	F	13FEB2021	68	Respiratory failure	COVID-19
	C4591001 1036 10361140∞#	2	91	M	10FEB2021	64	Road traffic accident	
	C4591001 1039 10391010∞	2	71	M	18NOV2020	85	Arteriosclerosis	Hypertensive heart disease
	C4591001 1066 10661350	1	16	M	03NOV2020	58	Myocardial infarction	
	C4591001 1084 10841266∞	2	121	M	12JAN2021	77	Sepsis	Emphysematous cholecystitis

Narrative Comment

Subject C4591001 1084 10841470, a 65-year-old white male with a pertinent medical history of hyperlipidemia and hypertension (since 2010) and pulmonary fibrosis (since 2014), received Dose 1 on 30 Sep 2020 and Dose 2 on 21 Oct 2020 (Day 22). The subject was diagnosed with COVID-19 infection and multiple organ dysfunction syndrome on 31 Dec 2020, 71 days after receiving Dose 2. On 23 Dec 2020 (Day 85), the subject received a prohibited vaccination (Moderna COVID-19 vaccine [mRNA-1273]) through his employer. The site was first informed of this vaccination by the subject's son on 07 Jan 2021 (Day 100).

Concomitant medications included ezetimibe/simvastatin (since 2010) for hyperlipidemia, omeprazole (since 2013) for gastroesophageal reflux disease, nebivolol hydrochloride (since 2015) for hypertension, and trazodone (since 2015) for insomnia.

The subject experienced shortness of breath, fever, cough, fatigue, and muscle aches "a day or so after" exposure to COVID-19 on 28 Dec 2020 (Day 90). On 31 Dec 2020 (Day 93), the subject received monoclonal antibodies from his primary care physician. Later the same day (Day 93), the subject presented to the emergency department with weakness, dyspnea, nausea, and diarrhea and was subsequently hospitalized with COVID-19. On the same day (Day 93), the subject's laboratory tests included: a positive SARS-CoV-2 test, sodium of 134 mmol/L (normal range [NR]: 137-145 mmol/L), chloride of 97 mmol/L (NR: 98-107 mmol/L), glucose of 121 mg/dL (NR: 74-99 mg/dL), aspartate aminotransferase of 78 (NR: 17-59, unit not provided), alanine aminotransferase of 51 (normal high: 50, unit not provided), C-reactive protein of 191.2 mg/dL (normal high: 10 mg/dL), total protein of 8.5 g/dL (NR: 6.3-8.2 g/dL), D-dimer quantitative of 1.21 µg/mL fibrinogen equivalent units (normal high: 0.50 µg/mL), red blood cell count of 5.86 M/mm3 (NR: 4.20-5.70 M/mm3), hemoglobin of 17.8 g/dL (NR: 13-17 g/dL), and hematocrit of 53.1% (NR: 40%-50%). The chest x-ray that same day (Day 93) was consistent with bilateral multifocal viral pneumonia. The subject was treated with ondansetron hydrochloride, dexamethasone, sodium phosphate, enoxaparin sodium, nebivolol hydrochloride, magnesium sulfate, trazodone, acetaminophen, magnesium oxide, potassium bicarbonate/citric acid, potassium chloride, pantoprazole, loperamide, melatonin, and vitamin D3. On 02 Jan 2021 (Day 95), the subject was treated at bedside for acute hypoxemic respiratory failure with a left radial arterial line placed, and he was intubated. After being placed on a ventilator, his health status continued to deteriorate, resulting in multiple organ dysfunction syndrome. On 04 Jan 2021 (Day 97), he suffered acute renal failure. Acute hypoxic respiratory failure and acute renal failure were considered because of the COVID-19. On 11 Jan 2021 (Day 104), the subject's family opted for "do-not-resuscitate" status. On 19 Jan 2021 (Day 112), the site learned that the subject had died on 11 Jan 2021 (Day 104), and it was unknown if an autopsy was performed. It was reported that the subject also experienced shock, nose bleeding, pulmonary fibrosis, hypertension, acute kidney injury, dyslipidemia, and gastroesophageal reflux disease. The cause of death was reported as disease progression, multiple organ dysfunction syndrome, and COVID-19 infection.

The subject's vaccine status was unblinded on 14 Jan 2021.

In the opinion of the investigator, there was no reasonable possibility that the COVID-19 infection and multiple organ dysfunction syndrome were related to the study intervention, concomitant medications, or clinical trial procedures. Multiple organ dysfunction syndrome was considered related to COVID-19. Pfizer concurred with the investigator's causality assessment.