Internal review 21/813

1. Introduction

Dear Dr Lee Proctor,

We are writing in response to your request for a review of the Medicines and Healthcare products Regulatory Agency's ('the Agency') reply to your FOI request 21/813. This is part 2/2 of the internal review.

The purpose of this review is to determine whether the Agency dealt properly and fairly with your request under the Freedom of Information Act (FOIA). In particular, it will examine the reasons why information was withheld from you.

Your original request and the Agency's response are annexed.

You stated in your request for this review that
"With the greatest respect I am aware of no authorised pharmaceutical products licensed in the UK for which the chemical structure of the active pharmaceutical ingredient (API) has been wilfully withheld from public disclosure due to the commercial interests of the pharmaceutical innovator. Commercial secrets and harm for any drug product will be comprehensively protected by the pharmaceutical innovator through multiple filings of intellectual property within all international patent jurisdictions. This is standard commercial practice.

The Pfizer and Moderna vaccines are a new class of mRNA vaccines. This type of vaccine has never previously been approved for human use before December 2020 when they received emergency authorisation for inoculation against SARS-CoV-2. The active pharmaceutical ingredient used in these vaccines is a nucleoside-modified mRNA that encodes for the Spike-protein antigen of SARS-CoV-2. These vaccines have been approved for use for any individual aged 16 or older. Most of the UK population is currently being inoculated and Government is mandating vaccination under certain circumstances and introducing an NHS vaccine passport system for certain social settings.

Given the millions of UK citizens who have and are being vaccinated and the measures Government are putting in place to ensure robust compliance then surely it is in the public interest to have complete transparency and for the public to know exactly the chemical structure of the API they are/have been inoculated with. This must surely exceed any commercial interests of the innovator especially when those commercial interests have full intellectual property protection. The chemical structure of the API is the full base sequence of the RNA used in both vaccines.

Similarly, the active pharmaceutical ingredient in the AstraZeneca and Johnson & Johnson vaccines are single recombinant DNA that encodes for the Spike-protein antigen. The DNA for both vaccines must undergo initial transcription within the nucleus of the cells of the recipient where it is transcribed into messenger RNA. The chemical structure of the API is the full base sequence of recombinant DNA.
I politely ask for the information in my original FOI request to be disclosed."

2. Consideration of the issues

Background
In the first phase of the internal review, we obtained consent from the relevant companies to release the nucleotide base sequences for COVID-19 vaccines Pfizer/BioNTech, COVID-19 Vaccine AstraZeneca, and COVID-19 Vaccine Janssen, and later followed the release of the sequence of the COVID-19 Vaccine Moderna. Following the receipt of these documents, you mentioned:

"However the document for the Janssen vaccine does not have the information I requested but instead contains information relating to the genetic sequence of the adenovirus vector (GenBank: EF153474.1) and the amino acid sequence for the protein of the immunogen. Can you kindly provide the full nucleotide base sequence for the dsDNA transgene that encodes for the immunogen because this is the active pharmaceutical ingredient in the Janssen vaccine."

Following this reply we confirmed:

"We have checked and confirm that the regulatory submission for Janssen does not contain the transgene nucleotide sequence. There is a full explanation of the molecular biology for the development of the plasmid, but the transgene sequence as a stand-alone is not provided."

To add clarification to the statement above, it should instead have read, 'does not contain the transgene *in a stand-alone* manner'.

We then took the step of re-contacting the company for representations in order to ascertain whether releasing the parts of the dossier related to the API alongside a further clarification / explanation of the active substance would be acceptable. The company replied to outline a real risk of commercial harm if this information was to be released. The arguments centred on the premise that the sequence (full nucleotide base sequence for the dsDNA transgene that encodes for the immunogen) was not available in the dossier in a stand-alone manner and was inseparable from other proprietary information. The assessment team that reviewed the quality aspects of the regulatory dossier, agreed with the arguments put forward by the company. To confirm, the nucleotide sequence we hold is in the form of a continuous sequence of c. 33,000 bases and there are no simple identifiers to discern where the gene encoding the immunogen portion begins.

When considering safety as a factor which is clearly in public interest, the assessment team noted that the requested part of the nucleotide sequence does not provide anything above and beyond that which is already provided in the publicly available assessment reports, known as PARs. They consolidated this view by placing an emphasis on the purposes of clinical trial data that help to support the product's benefit-risk, and the comprehensive safety surveillance strategy for monitoring the safety of all UK-approved COVID-19 vaccines, that the MHRA has in place.

In line with the above a decision was taken to uphold use of Sections 41 and 43(1) and (2) of the FOIA.

Has the Agency answered the request and have any exemptions been properly applied?

Section 41
Seeking a third-party perspective substantiates our position to uphold Section 41 and the arguments put forward in their correspondence with us, illustrated that the company are likely to mount legal actions against the MHRA were this information to be released—having made clear statements as to the confidential & commercially sensitive nature of the information.

Section 41 confers an absolute, rather than qualified exemption and there is no requirement to consider whether the public interest in maintaining the exemption outweighs the public interest in disclosure. However, ICO guidance is clear that for there to be an 'actionable' breach of confidence, the action for breach of confidence must be likely to succeed. We have therefore considered the public interest in disclosure in so far as it is relevant to identifying whether a public interest defence to an action for breach of confidence could exist and therefore whether disclosure would result in an actionable breach of confidence. We note that the test to establish whether a public interest defence for a breach of confidence exists does not function in the same way as the public interest test for qualified exemptions. However, we consider that similar public interest arguments apply to all exemptions applied in 21/813, therefore, to avoid duplication please also refer to table 1, below.

In terms of the public interest we do not perceive that our release of the information would outweigh the risk of a breach of confidence. To release proprietary information would likely undermine trust between the MHRA and the pharmaceutical company concerned. Further, because this internal review will be placed in the public domain it is reasonable to expect a form of *chilling effect*, where other companies also feel unable to place their trust in MHRA to keep their commercially sensitive information secure from competitors. A corollary is that if companies feel that their commercial activities are placed at risk, they could select to approach other markets rather than the UK/GB (outcomes that are not perceived to be in the public interest).

Table 1: Weighing the public interest in relation to Sections 41, 43(2), and (3)

Public Interest in favour of release	**Public Interest in favour of maintaining the FOIA exemption**
Increased transparency, and availability of additional data not already in the public domain. Deemed by the requester to help protect the public from unsafe products or dubious practices.	Relates to very specific aspect of the vaccine API i.e. full nucleotide base sequence for the dsDNA transgene that encodes for the immunogen. This information would not be expected to be understood by a lay audience. Further as described previously the clinical trial data and independent review of the vaccines by the Commission on Human Medicines supports the benefit risk of this

	COVID-19 vaccine.
Potential for a decrease rates of vaccine hesitation, as a portion of the public is known to be reassured by the general principle of information sharing.	Level of information in the public domain substantial, public assessment reports and details and data from COVID-19 pharmacovigilance / surveillance programme. Deemed proprietary information by company with tangible route to commercial harm, in terms, of a commercial advantage to competitors.
General educational interest to geneticists/biologists and vaccine developers	Quality assessment team confirmed that the dsDNA sequence is not pivotal to safety of the COVID-19 vaccine, which is instead predicated on the supportive data and information outlined in the Public Assessment Report [QA/biols to add]

We conclude that the public interest in releasing full nucleotide base sequence for the dsDNA transgene that encodes for the immunogen, is limited and does not outweigh the real risk commercial harm that was stipulated by the third party, and similarly does not outweigh the risk of detriment to the confider, if the information was to be released without their consent.

Has the Agency fulfilled its general obligation to be helpful?

An amicable tone was struck in the discourse related to the internal review, and the requester was kept informed of all developments. Aforementioned, steps were taken to contact the third party/s in relation to this request, a step which is not often undertaken in the context of the information sought, i.e. information that MHRA believes as pertains to information that is commercially sensitive as per the HMA guidance, see excerpt below:

"[…] only if it contains detailed information regarding new biologic active substances belonging to the class of recombinant proteins/polypeptides that reveals a trade secret (not patented), information on the amino acid sequence, should be regarded as CCI.

Notably, the requested nucleotide sequences have been provided for the three other COVID-19 vaccines (3/4), therefore, from a holistic perspective part I of this internal review actively fulfilled the most-part of the original request. However, we are aware that we have unfortunately been unable to provide the documents requested in your follow-up communication.

3. Conclusion and recommendations

We have noted a need to uphold use of Sections 41 and 43(1)* and (2)* in line with the representations made by the company, and a perceived greater risk of commercial harm vs. public interest.

*Section 43(1) provides an exemption from disclosure for information which is a trade secret.

*Section 43(2) exempts information whose disclosure would, or would be likely to, prejudice the commercial interests of any legal person (an individual, a company, the public authority itself or any other legal entity).

We apologise for being unable to release the data requested in your follow-up request, but we hope that the sequences that you have received thus far, will be of use/benefit to you. And, on this note, if you wished to describe further how these sequences will be used to support an argument in favour of improving public health or the safety of the vaccines / further arguments in the public interest. We may be able to alter our position on the full nucleotide base sequence for the dsDNA transgene that encodes for the immunogen i.e. the subject of your follow-up FOI request.

We would also like to mention that the COVID-19 vaccine Janssen is not in use in the UK, please see below:

https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting "*Three COVID-19 vaccines – the COVID-19 Pfizer/BioNTech Vaccine, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna – are currently being used in the UK*." (13 May update)

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

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: background correspondence

Prior correspondence related to this FOI and the internal review is located at the below link:
Full nucleotide base sequences for all of the COVID vaccines approved by the MRHA - a Freedom of Information request to Medicines and Healthcare Products Regulatory Agency - WhatDoTheyKnow