FOI 23-158 Yellow Card data

21 February 2023

Thank you for your detailed response to my FOI request 22/105, which I have reviewed.

There are a number of points I wish to address. I have done so below paragraph by paragraph

Or please advise whether I should submit each section separately, as a new request?

“All the COVID-19 vaccines used in the UK vaccination programme were approved following a rigorous review by the MHRA and the Government’s independent advisory body, the Commission on Human Medicines (CHM), of their safety, quality and effectiveness. The MHRA concluded that the COVID-19 vaccines were safe and effective and that the benefits outweigh any risk.”

- *Please provide direct links to the data used in the rigorous review by the MHRA and CHM?*

“No medicine or vaccine is completely risk-free and hence the MHRA continually monitors the safety of the COVID 19 vaccines through a comprehensive COVID-19 Vaccine Surveillance Strategy. This monitoring strategy is proactive and based on a wide range of information sources, with a dedicated team of scientists continually reviewing information to look for safety issues or any unexpected, rare events.

- *Please provide direct links to the above information sources, other than the Yellow Card Scheme, upon which Covid-19 Vaccine Surveillance is based; and has monitoring found any new safety issues or unexpected rare events?*

“The Yellow Card scheme is one of these sources of information and is the UK system for collecting suspected side effects to medicines and vaccines from healthcare professionals and patients. We publish a summary of Yellow Card reporting for the COVID-19 vaccines which summarises information received via the Yellow Card scheme. This report now focuses on the COVID-19 vaccines administered from the beginning of the Autumn 2022 booster campaign. Please see our existing record for a summary of information received via the Yellow Card scheme on COVID-19 vaccine primary and booster vaccination campaigns up to the end of August 2022 as well as safety investigations carried out by the MHRA on these products.”

- *Please provide full details, including the anonymised raw data, of the safety investigations carried out by the MHRA on these products. For example, any population-level statistical analyses or ecological analyses carried out in relation to fatal outcomes, myocarditis and pericarditis, menstrual disorders and pregnancy and the range of other isolated events or series of reports of serious suspected ADRs.*

“In terms of the probability of how likely it is that a report of a side effect is related to a COVID-19 vaccine, there is no defined list as such as many factors are considered. Yellow Card reports of suspected adverse drug reactions are evaluated, together with additional sources of evidence, by a team of safety experts to identify any new safety issues or side effects. We apply statistical techniques, known as disproportionality analyses, that can tell us if we are seeing more reports of an event for a particular vaccine compared to other vaccines. For these analyses, no specific temporal thresholds are used for time between vaccination and occurrence of event however the time to onset of the event after vaccination is taken into account as part of the overall assessment of any new safety signals. The assessment of any signals arising from these analyses aims to account for factors such as coincidental illness. We also look at the clinical characteristics to see if new patterns of illness are emerging that could indicate a new safety concern.”

- *Please provide the raw data used in the disproportionality analyses?*
- *What are the additional sources of evidence and have new safety issues or side effects been identified? Please provide all findings, including any new safety signals arising from the use of disproportionality analyses and whether clinical characteristics indicate new patterns of illnesses emerging?*

“As part of the enhanced surveillance strategy put in place for COVID-19 vaccines, additional statistical techniques are implemented where, for a number of adverse events of special interest, the number of reports received for each COVID-19 vaccine in compared to what we would expect to see given the extent of use of that vaccine, the age distribution of those who have received it, and the age-specific background rates of the event in the absence of vaccination. These observed versus. expected analyses do require a temporal threshold to be placed on the time between vaccination and occurrence of the event. The time chosen is event specific and dependent on the nature of the event. The default for proactive analyses is 45 days following each vaccine dose although sensitivity analyses including shorter and longer time intervals of 7 and 90 days are conducted. Further ad hoc analyses with differing time windows can be conducted as necessary. Multiple observed versus expected analyses are conducted allowing for differing levels of reporting, assuming 10%, 25%, 50%, and 100% of events occurring in the time window are reported to the Yellow Card scheme respectively.”

- *How are the age-specific background rates referred to above obtained?*
- *With regard to temporal thresholds, please can you clarify whether the temporal thresholds referred to are before an event is classified as an AE, or beyond which an event is not classified as an AE.*
- *what, if any, is the temporal threshold for the duration needed to elapse after injection before an event will be considered as an AE?*
- *How many Yellow Card reports of adverse events of special interest has the MHRA followed up?*

“We supplement this form of safety monitoring with other epidemiology studies including analysis of anonymised GP-based electronic healthcare records and other healthcare data to proactively monitor safety. These analyses are more bespoke and do not rely on reporting. Combined safety data enables the MHRA to detect side effects or safety issues associated with COVID-19 vaccines. We also work closely with our public health partners in reviewing the effectiveness and impact that the vaccines are having to ensure benefits continue to outweigh any possible side effects. In addition, we work with our international counterparts to gather information on the safety of vaccines in other countries.”

- *Please provide full details of the anonymised GP based electronic healthcare records and other healthcare data used to supplement safety monitoring.*

“For the vast majority of people, the benefits of the vaccines in preventing serious complications associated with COVID-19, far outweigh any currently known side effects. The safety of COVID-19 vaccines is continuously monitored; should a new safety issue be confirmed we will continue to act promptly to inform patients and healthcare professionals and take appropriate steps to mitigate any identified risk and protect public health.”

- *Please confirm the date when the use of AZ was stopped for all age groups in the UK, what actions the MHRA took to inform patients and healthcare professionals and the steps taken to mitigate any identified risk and to protect public health?*

MHRA RESPONSE

23 March 2023

Thank you for your further information request dated 21 February 2023 where you asked the following:

1. “All the COVID-19 vaccines used in the UK vaccination programme were approved following a rigorous review by the MHRA and the Government’s independent advisory body, the Commission on Human Medicines (CHM), of their safety, quality and effectiveness. The MHRA concluded that the COVID-19 vaccines were safe and effective and that the benefits outweigh any risk.”
    - *Please provide direct links to the data used in the rigorous review by the MHRA and CHM?*

2. “No medicine or vaccine is completely risk-free and hence the MHRA continually monitors the safety of the COVID 19 vaccines through a comprehensive COVID-19 Vaccine Surveillance Strategy. This monitoring strategy is proactive and based on a wide range of information sources, with a dedicated team of scientists continually reviewing information to look for safety issues or any unexpected, rare events.”
    - *Please provide direct links to the above information sources, other than the Yellow Card Scheme, upon which Covid-19 Vaccine Surveillance is*

based; and has monitoring found any new safety issues or unexpected rare events?

3. The Yellow Card scheme is one of these sources of information and is the UK system for collecting suspected side effects to medicines and vaccines from healthcare professionals and patients. We publish a summary of Yellow Card reporting for the COVID-19 vaccines which summarises information received via the Yellow Card scheme. This report now focuses on the COVID-19 vaccines administered from the beginning of the Autumn 2022 *booster* campaign. Please see our existing record for a summary of information received via the Yellow Card scheme on COVID-19 vaccine primary and booster vaccination campaigns up to the end of August 2022 as well as safety investigations carried out by the MHRA on these products."
    - *Please provide full details, including the anonymised raw data, of the safety investigations carried out by the MHRA on these products. For example, any population-level statistical analyses or ecological analyses carried out in relation to fatal outcomes, myocarditis and pericarditis, menstrual disorders and pregnancy and the range of other isolated events or series of reports of serious suspected ADRs.*

4. "In terms of the probability of how likely it is that a report of a side effect is related to a COVID-19 vaccine, there is no defined list as such as many factors are considered. Yellow Card reports of suspected adverse drug reactions are evaluated, together with additional sources of evidence, by a team of safety experts to identify any new safety issues or side effects. We apply statistical techniques, known as disproportionality analyses, that can tell us if we are seeing more reports of an event for a particular vaccine compared to other vaccines. For these analyses, no specific temporal thresholds are used for time between vaccination and occurrence of event however the time to onset of the event after vaccination is taken into account as part of the overall assessment of any new safety signals. The assessment of any signals arising from these analyses aims to account for factors such as coincidental illness. We also look at the clinical characteristics to see if new patterns of illness are emerging that could indicate a new safety concern."
    - *Please provide the raw data used in the disproportionality analyses.*
    - *What are the additional sources of evidence and have new safety issues or side effects been identified? Please provide all findings, including any new safety signals arising from the use of disproportionality analyses and whether clinical characteristics indicate new patterns of illnesses emerging?*

5. As part of the enhanced surveillance strategy put in place for COVID-19 vaccines, additional statistical techniques are implemented where, for a number of adverse events of special interest, the number of reports received for each COVID-19 vaccine in compared to what we would expect to see given the extent of use of that vaccine, the age distribution of those who have received it, and the age-specific background rates of the event in the absence of vaccination. These observed versus. expected analyses do require a temporal threshold to be placed on the time between vaccination and occurrence of the event. The time chosen is event specific and dependent on

the nature of the event. The default for proactive analyses is 45 days following each vaccine dose although sensitivity analyses including shorter and longer time intervals of 7 and 90 days are conducted. Further ad hoc analyses with differing time windows can be conducted as necessary. Multiple observed versus expected analyses are conducted allowing for differing levels of reporting, assuming 10%, 25%, 50%, and 100% of events occurring in the time window are reported to the Yellow Card scheme respectively."

- *How are the age-specific background rates referred to above obtained?*
- *With regard to temporal thresholds, please can you clarify whether the temporal thresholds referred to are before an event is classified as an AE, or beyond which an event is not classified as an AE.*
- *what, if any, is the temporal threshold for the duration needed to elapse after injection before an event will be considered as an AE?*
- *How many Yellow Card reports of adverse events of special interest has the MHRA followed up?*

6. "We supplement this form of safety monitoring with other epidemiology studies including analysis of anonymised GP-based electronic healthcare records and other healthcare data to proactively monitor safety. These analyses are more bespoke and do not rely on reporting. Combined safety data enables the MHRA to detect side effects or safety issues associated with COVID-19 vaccines. We also work closely with our public health partners in reviewing the effectiveness and impact that the vaccines are having to ensure benefits continue to outweigh any possible side effects. In addition, we work with our international counterparts to gather information on the safety of vaccines in other countries."
    - *Please provide full details of the anonymised GP based electronic healthcare records and other healthcare data used to supplement safety monitoring.*

7. "For the vast majority of people, the benefits of the vaccines in preventing serious complications associated with COVID-19, far outweigh any currently known side effects. The safety of COVID-19 vaccines is continuously monitored; should a new safety issue be confirmed we will continue to act promptly to inform patients and healthcare professionals and take appropriate steps to mitigate any identified risk and protect public health."
    - *Please confirm the date when the use of AZ was stopped for all age groups in the UK, what actions the MHRA took to inform patients and healthcare professionals and the steps taken to mitigate any identified risk and to protect public health?*

We can confirm that we hold some of the information you have requested. However, our assessment of your request is that Section 12(1) of the Freedom of Information Act applies, and we cannot proceed any further. Section 12 of the Act allows public authorities to refuse requests where the cost of dealing with them would exceed the appropriate limit, which for central government is set at £600. This represents the estimated cost of one person spending 24 working hours in determining whether the department holds the information, locating, retrieving and extracting the information. We consider that this specifically applies to the following elements of your request:

- Please provide full details, including the anonymised raw data, of the safety investigations carried out by the MHRA on these products. For example, any population-level statistical analyses or ecological analyses carried out in relation to fatal outcomes, myocarditis and pericarditis, menstrual disorders and pregnancy and the range of other isolated events or series of reports of serious suspected ADRs.

- Please provide the raw data used in the disproportionality analyses.

- What are the additional sources of evidence and have new safety issues or side effects been identified? Please provide all findings, including any new safety signals arising from the use of disproportionality analyses and whether clinical characteristics indicate new patterns of illnesses emerging?

- How many Yellow Card reports of adverse events of special interest has the MHRA followed up?

Although we hold information on whether a Yellow Card report has been followed up, this information is not easily extractable. The MHRA has received over 470,000 Yellow Card reports associated with a COVID-19 vaccines. An individual would need to manually open each Yellow Card report to check whether a request for further information was sent. Checking a single Yellow Card report for evidence of follow up would take a minimum of 45 seconds and in some instances longer. This would equate to an individual spending over 5875 hours for this aspect of your request alone.

In line with Section 16 of the Act, we have a duty to help you refine your request. However, given the amount of data you have requested it is difficult for us to help suggest refinement at this point. As a starting point you may wish to decide which of the bullet points, we have listed above are of greatest interest to you, we will then try and suggest refinement.

Please note that in relation to point 1, we consider that we have addressed this in a previous reply to you of 09 March (attached for reference).

In relation to point 7, this is not data which we hold. The body responsible for advising the UK Government on the COVID-19 vaccine roll out is the Joint Committee on Vaccination and Immunisation (JCVI). JCVI advice is independent of MHRA. You may wish to contact the JCVI. Please note that this vaccine continues to hold a marketing authorisation in the UK.

We hope this information is helpful.
If you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within two months of the date you receive this response and addressed to: info@mhra.gov.uk
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

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