



Medicines & Healthcare products Regulatory Agency

Nick xxxx

MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

www.gov.uk/mhra

13 July 2022

MHRA reference: FOI 22/562 internal review

Dear Mr xxxx,

I am 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 (22/562).

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. You originally requested the following:

- a) the document which describes your process for analysis of Yellow Card reports; and
- b) the most recent audit report of MHRA's safety management of medicines.

Having investigated the original handling of the FOI response, I have concluded that the Agency's position is upheld. Information that the Agency holds, which was deemed to fulfil your request, was provided. The internal review only requires a review of the handling of the original request. There is no obligation for an explanation to be provided or for us to create new information under the FOIA. However, I will address the points you made in your request for an internal review.

- a) you withheld all but 5 pages of the 50 page audit report, on the grounds that the rest of the report does not relate to 'safety management of medicines'. However, as the Executive Summary (page 4) rightly says, ISO9001 certification depends on the connectivity between all of your processes. I therefore still wish to see the complete report;



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We have provided the information requested in the original request (most recent audit report of MHRA's safety management of medicines). If you wish to request the whole ISO report this can be done under a new, separate request

b) the Audit was against the requirements of ISO9001. That is a Quality Management standard not a Safety Management standard. You therefore also need to explain why an audit of your Quality Management System provides you with assurance about the effectiveness of your Safety Management (of medicines);

Please note that 'ADR reporting and signal management for medicinal products' are core activities and within the scope of MHRA ISO 9001 certification as 'perform post market surveillance'.

c) the Audit you attached was dated Feb 20. However, you have a statutory obligation under the Human Medicines Regulations to audit your pharmacovigilance system every two years. So, even if you are satisfied that a QMS audit meets that requirement (b) above), you either have a more recent audit report or you must explain why more than two years have elapsed without the required audit;

A planned deviation of audits was agreed due to COVID-19 since business continuity procedures were in operation.

d) you attached your process for 'Signal Assessment and Signal Detection Meetings (VIRG0603)'. That met the part of my request about signal/trend analysis/investigation. However, you did not provide a copy of your process for investigation of individual Yellow Card reports (which was also explicitly part of my FOI request);

As you are aware, the MHRA assesses the balance of risks and benefits of all medicines and vaccines at the time of initial licensing and throughout their use in clinical practice. Part of our monitoring role includes reviewing reports of suspected side effects received via the Yellow Card scheme. We carefully evaluate reports of suspected side effects as soon as they are received to consider whether the medicine or vaccine may have caused the event, or whether the event was likely to be purely coincidental. We do so by considering all available evidence, through the procedure described in VIRG0603 which has been previously provided to you. Coroners are independent judicial officers who investigate deaths reported to them. They will make whatever inquiries are necessary to find out the cause of death, this includes ordering a post-mortem examination, obtaining witness statements and medical records, or holding an inquest. As such, the MHRA do not hold a process for investigation of individual Yellow Card reports as it is the role of the coroner to determine the likely cause of death on a case by case basis. It is not the role of the MHRA to adjudicate on individual events as we assess the body of evidence as a whole.

e) also in relation to VIRG0603, your covering letter states that "...substantial adjustments were made associated with Covid-19". Please can you confirm that the version of VIRG0603 you attached (Jul 20) incorporates those changes or that they are still outstanding.

COVID-19 specific procedures were not requested in the original request. This would typically need to be handled as a new request. However, in the interest of being helpful we have provided our latest guidance document which reflects current approach for these products.



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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

Chris Penny
MHRA Customer Experience Centre Performance Manager

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Annex A: Background correspondence

Original FoI Request and Agency response on 23rd May 2022

Dear Mr xxxx,

RE: FOI 22/562

Thank you for your email correspondence with our FOI team on the 18 March 2022 and please accept our sincerest apologies for the delay in responding to your FOI request. It was noted in your email that you specifically requested the following:

- a) the document which describes your process for analysis of Yellow Card reports; and
- b) the most recent audit report of MHRA's safety management of medicines.

To provide some background, the Yellow Card scheme, which is run by the Medicines and Healthcare products Regulatory Agency (MHRA), is the UK programme for collecting experiences of side effects from healthcare professionals and patients and is used to monitor the safety profile of all medicines, including those from prescriptions, over-the-counter or general retail sales. Reports are also received for herbal medicines and other unlicensed medicines. It is a voluntary scheme for healthcare professionals and members of the public; however, there is a legal requirement for pharmaceutical companies to report side effects that they have received to the scheme.

While a significant proportion of the population will gain benefit from taking a medicine and experience no serious adverse effects, there will always be a proportion of individuals who will suffer a side effect as a direct result of taking a medicine. Since the difference in individuals' responses results from differences in their genetic and environmental circumstances one of the MHRA's roles is to ensure that as much relevant information as possible about a serious suspected adverse drug reaction is gathered to enable an informed judgement about causality to be made i.e. whether the medicine could be directly responsible for causing the reaction.

The MHRA assesses the balance of risks and benefits of all medicines and vaccines at the time of initial licensing and throughout their use in clinical practice. Where appropriate, the MHRA seeks advice from the independent Commission on Human Medicines (CHM). All reports received are entered onto our database for rapid analysis, allowing us to identify potential new safety concerns. We supplement this form of safety monitoring with clinical trial data, data from other regulatory authorities worldwide, literature reports, epidemiology studies and other healthcare data to proactively monitor safety. When a new side effect is identified, information is carefully considered in context of the overall side effect profile for the medicine, and how it compares with other medicines used to treat the same condition.



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We also consider the international experience based on data from other countries. As well as confirming new risks, an equally important objective of monitoring will be to quickly rule out risks – in other words, to confirm that the medicine or vaccine is not responsible for a suspected side effect and to provide reassurance on its safety.

The MHRA carefully evaluates reports of serious suspected side effects as soon as they are received to consider whether the medicine or vaccine may have caused the event, or whether the event was likely to be purely coincidental. Additionally, we apply statistical techniques and epidemiological analysis that can tell us if we are seeing more events than we would expect to see, based on what is known about background rates of illness in the absence of vaccination. This aims to account for factors such as coincidental illness. It is important to understand that the possible adverse effects must be balanced against the benefits of using this medicine or vaccine. Therefore, any potential adverse effects need to be viewed in light of the numbers of people who have taken the medicine without developing side effects. The safety of all medicines has been closely monitored by the MHRA since first authorisation.

Further to your specific request for the documents we follow for analysis of Yellow Cards, please find enclosed our System Operating Procedure (SOP) which describes the steps we follow as detailed above whilst carrying out our Signal Assessment of Adverse Drug Reaction (ADR) reports. Please note that substantial adjustments were made to Agency operating procedures regarding the assessment of ADR reports associated with COVID-19 related products to allow for more rapid analysis whilst maintaining usual assessment standards.

In terms of your additional request for the most recent audit report, please find enclosed an assessment report from our most recent external audit, conducted 28 January 2020 to 10 February 2020. I can confirm the SOP provided in response to the initial part of your request was in the scope of this audit. Please note that any information not relevant to your request (safety management of medicines) has been removed from the report.

I hope the information provided is helpful, but 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 of this response; and can be addressed to this email address.

Yours sincerely,

FOI Team,

Vigilance and Risk Management of Medicines Division



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From: Nick xxxx> _____
Sent: 18 March 2022 07:56
To: MHRA Customer Services <MHRACustomerServices@mhra.gov.uk>
Subject: FOI 22/562 - FOI Request - Safety-related Documentation

This is a Freedom Of Information request. Please can you provide :

- a) the document which describes your process for analysis of Yellow Card reports; and
- b) the most recent audit report of MHRA's safety management of medicines.

For the avoidance of doubt, on a), I do not want or expect a narrative answer. Rather, I am requesting the relevant MHRA internal document(s) which instructs/guides your own staff about, inter alia, who conducts the investigation/analysis (of both individual YC reports and of trends/signals), how it is done, what timescales, how frequently, reporting the findings to whom, and the process for those findings being reviewed/acted upon by senior staff, including reporting to DHSC and others.

I would also note that both a) and b) are made publicly available by other areas of Government which also regulate safety critical sectors (such as aviation, nuclear and weapons).

Regards, Mr xxxx



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Request for an internal Review dated 24th May 2022

From: Nick xxxx> _____
Sent: 24 May 2022 11:10
To: Pharmacovigilanceservice <Pharmacovigilanceservice@mhra.gov.uk>
Cc: MHRA Customer Services <MHRACustomerServices@mhra.gov.uk>; FOI_Policy <FOI_Policy@mhra.gov.uk>
Subject: Re: FYI - FOI 22/562 - FOI Request - Safety-related Documentation

Dear Sir/Madam,

Thank you for your very belated response (23 May 22) to my FOI request (22/562, 18 Mar 22). It is still unclear why I had to submit two complaints to the Information Commissioner to elicit any response from you.

This email is to request an Internal Review because your response does not fully meet my request. Specifically :

a) you withheld all but 5 pages of the 50 page audit report, on the grounds that the rest of the report does not relate to 'safety management of medicines'. However, as the Executive Summary (page 4) rightly says, ISO9001 certification depends on the connectivity between all of your processes. I therefore still wish to see the complete report;

b) the Audit was against the requirements of ISO9001. That is a Quality Management standard not a Safety Management standard. You therefore also need to explain why an audit of your Quality Management System provides you with assurance about the effectiveness of your Safety Management (of medicines);

c) the Audit you attached was dated Feb 20. However, you have a statutory obligation under the Human Medicines Regulations to audit your pharmacovigilance system every two years. So, even if you are satisfied that a QMS audit meets that requirement (b) above), you either have a more recent audit report or you must explain why more than two years have elapsed without the required audit;

d) you attached your process for 'Signal Assessment and Signal Detection Meetings (VIRG0603)'. That met the part of my request about signal/trend analysis/investigation. However, you did not provide a copy of your process for investigation of individual Yellow Card reports (which was also explicitly part of my FOI request);

e) also in relation to VIRG0603, your covering letter states that "...substantial adjustments were made associated with Covid-19". Please can you confirm that the version of VIRG0603 you attached (Jul 20) incorporates those changes or that they are still outstanding.

Yours faithfully
Mr xxx