

**COMMISSION ON HUMAN MEDICINES (CHM)
COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP**

Minutes of the meeting held on **Wednesday 8th June 2022** at **10:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer¹
Mr VI G Fenton-May
Professor N French²
Professor D Goldblatt
Ms S Hunneyball
Professor K Hyrich
Professor P J Lehner
Mr R Lowe
Dr S Misbah
Professor Y Perrie
Professor S Price
Professor C Robertson³
Professor K M G Taylor⁴
Dr R Thorpe
Professor S Walsh
Mrs M Wang

Apologies

Professor G Dougan
Sir M Jacobs
Professor H J Lachmann
Dr A Riordan
Professor M Turner
Professor C Weir

Invited Expert⁵

[REDACTED]
[REDACTED]

Observers

[REDACTED]
[REDACTED]
Professor W S Lim

[REDACTED]
[REDACTED]

Secretariat

[REDACTED]
[REDACTED]

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea - LD
[REDACTED] - VRMM

Presenters supporting specific items

[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] - VRMM
Mr P Tregunno - VRMM

MHRA Observers

[REDACTED] - VRMM
[REDACTED] - MHRA-Policy
[REDACTED] - VRMM
[REDACTED] - VRMM
[REDACTED] - VRMM
[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] - LD
[REDACTED] - VRMM

Government Legal

[REDACTED]

¹ left during item 3
² joined at item 4
³ left during item 4
⁴ left at item 5
⁵ joined for item 2 only

Key

LD = Licensing Division
VRMM = Vigilance & Risk Management of Medicines

[REDACTED]

5th May 2023

1. Introduction and Announcement

1.1 The Chair reminded Members, invited Experts and observers that the content of papers and proceeding of the meeting are strictly confidential and should be treated as ‘Official – sensitive commercial’ and should not be disclosed. There is no consent for members / participants to record the meeting, take screenshots or photographs of presentations. The meeting was recorded by the MHRA Secretariat for minute taking purposes only. The Chair & Members including all participants gave full consent to the recording prior to the start of the meeting.

1.2 Conflict of Interest Policy (Annex I to the minutes)

The Chair reminded members and participants that, in accordance with the CHM Code of Practice, they should declare any financial interests (personal or non-personal, specific or non-specific) which they have, or which an immediate family member has, in any of the agenda items. Members were also reminded to declare any other matter which could reasonably be perceived as affecting their impartiality.

1.3 Participants declared interests and other relevant interests for this meeting listed at **Annex II** to the minutes.

1.4 Apologies were received from Professors Dougan, Lachmann, Turner, Weir, Dr Riordan and Sir Michael Jacobs for this meeting.

1.5 The Chair welcomed the following invited experts to the meeting:

[REDACTED]
[REDACTED] Bristol Heart Institute

[REDACTED]
[REDACTED] University of
Cambridge [REDACTED]
[REDACTED]

1.6 The Chair welcomed the following observers to the meeting:

[REDACTED]
[REDACTED] Public Health Scotland

[REDACTED]
NHS England Medical Director [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Professor Wei Shen Lim
Chair of JCVI

[REDACTED]
Public Health England

[REDACTED]
[REDACTED]
NHS England and NHS Improvement (National)

2. Myocarditis report from an Inquest

- 2.1** The EWG was informed that, in May 2022, the MHRA had become aware of an article in a national newspaper reporting that a previously well 36-year-old female had died suddenly at home, 11 days after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine. The death had occurred in June 2021 with a Coroner’s Inquest conducted in May 2022, to which the MHRA had not been invited to give evidence. The Inquest recorded the cause of death as 1a. acute myocarditis and 1b. recent COVID-19 immunisation. A Yellow Card was never submitted.
- 2.2** The MHRA had subsequently received the case disclosure for the Inquest, including the post-mortem examination report, the record of the Inquest and evidence from healthcare professionals and emergency services staff involved in the death. The MHRA had also contacted the pathologist who conducted the post-mortem examination to ask a series of follow-up questions.
- 2.3** The MHRA described all the available evidence to the EWG and noted that the single small focus of myocarditis identified post-mortem was initially considered by the pathologist to be too small to explain the sudden cardiac death. The MHRA concluded that the official cause of death of acute myocarditis secondary to COVID-19 vaccination was not supported by the post-mortem findings and that expert cardiology advice was considered necessary.
- 2.4** The EWG was asked to advise on the strength of the evidence for a causal relationship between COVID-19 vaccination and the sudden death, what information should additionally be sought and whether it had any other comments or recommendations.
- 2.5** The EWG, including invited cardiology experts, commented that the follow-up questions sent by MHRA to the pathologist were appropriate. The EWG noted that the location of the focal myocarditis in this case was not known, and this was relevant to understanding the risk of arrhythmia. It further commented that cardiac pathology is a highly specialised field requiring analysis by relevant experts, which had not happened in this case and should be sought. Full genetic, antimicrobial and molecular testing was recommended including screening of the patient’s family for possible inherited cardiac disorders. Noting some abnormalities of the lung and kidney, the EWG recommended that saved serum should be tested for vasculitis-related antibodies. The EWG recommended that MHRA obtain a transcript of the Inquest. Overall, the EWG could not make a definitive statement about causality due to the absence of key information.

3. Review of COVID-19 vaccines and Long COVID

- 3.1** The EWG was presented with a review of the Yellow Card reports of suspected long COVID following vaccination with AstraZeneca, Moderna and Pfizer COVID-19 vaccines up to 18 February 2022 as well as information available in the literature.
- 3.2** The EWG was informed that all reports mentioning “long” “COVID” in the narrative were reviewed. The majority of these reports reported a prior COVID-19 infection as well as a history of long COVID. In most of these reports the patient did not mention any effect from the vaccine on their long COVID symptoms, and the information was included as past medical history. Some patients reported a worsening of their long COVID symptoms following vaccination and some reported an improvement. There were some reports with

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no known COVID-19 infection where patients are experiencing a range of long-term effects following the COVID 19 vaccination.

3.3 The EWG were also presented with a review of the literature. It was noted that there are no published case reports of long COVID following vaccination. However, there are several studies showing that 2 doses of the vaccine reduce the self-reporting of long COVID following COVID-19 infection.

3.4 The EWG noted that the data was generally reassuring. It was noted that long COVID is a heterogeneous collection of conditions and that there is cross over with other conditions such as chronic fatigue and fibromyalgia. From the reports reviewed, a possible alternative explanation could not be ruled out and therefore an association could not be considered established.

4. COVID-19 Surveillance Strategy Review

4.1 The EWG were presented with a paper summarising the activities conducted under the MHRA's COVID-19 vaccine surveillance strategy. The paper outlined the work conducted under each of the four elements of the strategy and the successes and challenges with its delivery.

4.2 The paper highlighted the substantial experience gained on products used within the UK vaccination campaign since it commenced in December 2020, and the change in the COVID-19 environment over the course of that time. Based on the knowledge of the products currently in use, the MHRA proposed now was an appropriate time to review the surveillance strategy and plan for a potential Autumn vaccination campaign.

4.3 The paper noted the potential for variant strains of existing vaccines, bi-valent, multi-valent and combination vaccines in the future, as well as existing authorised products that have not been used within the UK programme, and that the surveillance strategy needed to take account of the UK and international experience with different products.

4.4 It was highlighted that the MHRA's response also needed to be proportionate and aligned with the Government 'Living with COVID-19' strategy

4.5 In setting out the proposed approach to surveillance, the paper highlighted that the MHRA had already specified to NHS-Digital and the Public Health Agencies that requirement for provision of vaccination records from point of care systems to electronic healthcare records and near real time usage data would be maintained and that these elements would enable MHRA to scale up and down surveillance activities as required.

4.6 The paper proposed that it was an appropriate time to begin transition away from the COVID-19 specific Yellow Card reporting systems and to publicise the main Yellow Card site from the Autumn. It was noted that the Yellow Card site now has substantially enhanced functionality, meaning that passive surveillance, active follow up and active surveillance would all be feasible from the same platform. It was noted that the MHRA can deploy smart reporting forms based on conditional logic and automate follow up based on identified risks should the need arise.

4.7 A rationalisation of the epidemiological approaches deployed was also proposed, with a pause on the proactive elements of the current strategy, on the understanding that they could be restarted in the event of a significant change to the vaccine programme or new safety concern.

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- 4.8 It was proposed that COVID-19 vaccines should be included within an extended enhanced surveillance approach to the routine seasonal flu programme, including routine monitoring of an extended list of Adverse Events of Special Interest (AESI).
- 4.9 The paper proposed continued use of national and international networks on an ad-hoc basis to support surveillance, given the significant value of international data and experience in assessment of issues through the vaccination campaign to date.
- 4.10 It was noted that there are now more robust sources of evidence than spontaneous reports assessed against case definitions for the safety concerns where this has been one of the tools used for their assessment. As such it was recommended to phase out such activities, with the knowledge that they could be reinstated if necessary.
- 4.11 Given reducing numbers of vaccinations, and associated reporting of side effects it was proposed to begin a phased reduction in the frequency of publication of the Weekly ADR report, initially to twice weekly, and then to monthly before implementation of a new quarterly format by the end of the year.
- 4.12 The Vaccine Benefit-Risk EWG endorsed the proposals in the paper for a phased transition and agreed that systems and approaches could be used for other products in future. The EWG were also supportive of scientific publications in relation to methodologies employed and recommended that communication of changes in frequency of weekly publication could be highlighted within the report itself.
- 4.13 Members noted the volume, breadth and quality of the work that had been completed under the strategy.
- 4.14 The EWG advised that they support the recommendations within the paper.

5. **Vaxzevria Annual Renewal**

5.1 [Redacted content]

6. **Any Other Business**

None.

7. **Date and time of next meeting**

The next meeting has been scheduled for **Thursday 23rd June 2022 at 10:30.**

The Meeting today started at 10:31 and ended at 12:32.

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Annex I

Conflict of Interest Policy for CHM COVID-19 Vaccine Benefit Risk EWG

Chair and Members

- May not hold current personal interests in one or more companies associated with the development of COVID-19 vaccines
- May not currently be or have previously been involved in the development of COVID-19 vaccines

Invited to all meetings, receives all papers and presentations and is permitted full participation in discussion, including drawing up conclusions and recommendations

Invited experts

- May hold current personal interests in one or more companies associated with the development of COVID-19 vaccines
- May currently be or have previously been involved in the development of COVID-19 vaccines

May be invited to all relevant meetings, receives all papers and presentations and is permitted to participate in discussions when invited by the Chair. Does not contribute to conclusions and recommendations

Observers

Are invited to attend all meetings. Will not participate in drawing up conclusions and recommendations.

Annex II

The following participants declared interests and other relevant interests at the meeting today:

Professor Sir Munir Pirmohamed - NPNS AstraZeneca - Research grant to UOL to support PhD in drug interactions.

Other relevant interests in Pfizer, Janssen, Sanofi – Sir Munir is part of an EU-funded IMI consortium on gene therapy, and these companies are partners in the project. The University of Liverpool will get funding from the EU (but not from the partners), this IMI project commences on 3rd November 2020.

AGILE – this is a Liverpool early phase trial platform (between University of Liverpool and Liverpool School of Tropical Medicine). It is funded by the Wellcome Trust and UKRI/DHSC/NIHR. It is NOT evaluating vaccines, but only drugs to treat COVID-19. Sir Munir is not on the trial management group, and he is not directly involved in choosing the compounds for the study. Sir Munir has no involvement with any of the developers of the compounds to be studied (academic or industrial).

Sir Munir is a member of the UK COVID Therapeutics Advisory Panel (UK-CTAP), which is advising the CMO on which compounds need to be prioritised for the RECOVERY+ trial (RECOVERY is funded via NIHR/DHSC).

Professor Breuer– NPNS – Professor Breuer is on the data safety monitoring committee, DSMB, a study looking at combining vaccines being run by Matthew Snape in Oxford. There does not appear to be any involvement of the vaccine manufacturers and is for already licensed vaccines. The study is funded by the NIHR (Dec 2020).

Professor French - Other relevant interest - Provides clinical care when in covering the acute medical wards where patients with COVID-19 are cared. NPNS in GSK - In September 2020 a sub-contract was signed with the Liverpool School of Tropical Medicine to undertake work evaluating the safety and effectiveness of GSK's RTS's malaria vaccine in Malawi. GSK are the primary funders to the LSTM.

Ms Hunneyball - Other relevant interest – writes articles published in the Chemist and Druggist magazine, a trade magazine for pharmacists, but receives no payment for these articles. The information referred to in the articles is in the public domain. Ms Hunneyball makes it clear that these are her personal views and reflections and references all sources of information used.

Professor Hyrich – NPNS - Professor Hyrich was co-I on an investigator-initiated research grant exploring predictors of outcome in rheumatoid arthritis. NPNS Pfizer- she is a Co-I on a grant exploring adherence to JAK inhibitors in rheumatoid arthritis. NPNS in Abbvie, Professor Hyrich gave some lectures at an education conference on effectiveness of treatment for rheumatoid arthritis.

Professor Lehner - Other relevant interest – Professor Lehner previously held a DPAC (Discovery Partnership with Academia) agreement with GSK, but this has been completed. Professor Lehner's participation in his local hospital D and T governance committee deliberations would form the normal activity and professional responsibility in his post and does not interfere with the EWG considerations (Sept 2020).

Dr Misbah - NPNS - Holds honorary Senior Lectureship with University of Oxford & Oxford University Hospitals NHS Foundation Trust.

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Professor Perrie - NPNS in Pfizer & AstraZeneca arising from a contract for a grant (March 2018), which includes contributions from these companies to the University of Strathclyde, Janssen in writing a grant for a PhD (now funded), GSK – arising from an EU grant to University of Strathclyde (Jan 2019-Dec 2019).

Professor Price - NPNS in GSK and AstraZeneca – which relates to donations provided by both companies to the British Toxicology Society (BTS) to support their Annual Congress and Education and Training of which Professor Price is currently President of the Society (2020-2022).

Mrs Wang - Other relevant interests arising from being highly sensitive to insect stings, and plant products such as Hyacinth bulbs, as recorded on Mrs Wang's medical records. The family of Mrs Wang lives with several rare diseases and conditions, some of which result in epileptic fits.

Observers

██████████ - NPNS interest as the institution ██████ works for (Nottingham University Hospitals NHS Trust) has received unrestricted investigator-initiated research funding from ██████ for an unrelated prospective population-based cohort study of pneumococcal pneumonia ██████.

██████████ – Other relevant interest in Pfizer & GSK. The Immunisation and Countermeasures Division has provided vaccine manufacturers (including Pfizer and GSK) with post-marketing surveillance reports on pneumococcal and meningococcal infection which the companies are required to submit to the UK Licensing authority in compliance with their Risk Management Strategy. A cost recovery charge is made for these reports.