

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

Minutes of the meeting held on **Friday 4th February 2022** at **11:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor G Dougan
Mr VI G Fenton-May
Professor N French
Ms S Hunneyball
Professor K Hyrich
Professor H J Lachmann¹
Professor P J Lehner
Mr R Lowe
Dr S Misbah
Professor Y Perrie
Professor S Price
Dr A Riordan
Professor C Robertson
Professor T Solomon²
Professor K M G Taylor
Dr R Thorpe
Professor M Turner
Professor S Walsh
Mrs M Wang
Professor C Weir

Apologies

[REDACTED]
[REDACTED]
[REDACTED]

Invited Experts³

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Observers

[REDACTED]
[REDACTED]
Professor WS Lim

Secretariat

[REDACTED]
[REDACTED]

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea – LD
[REDACTED] – VRMM⁴

Presenters supporting specific items⁴

[REDACTED] - LD
[REDACTED] – LD
[REDACTED] – VRMM
[REDACTED] – VRMM
[REDACTED] – VRMM
[REDACTED] - LD

MHRA Observers

[REDACTED] - LD
Dr A Cave – Chief Safety Officer
[REDACTED] - MHRA-Policy
[REDACTED] - Comms
[REDACTED] - VRMM
[REDACTED] - LD
Ms N Rose – MHRA-NIBSC
[REDACTED] - VRMM
Mr P Tregunno - VRMM
[REDACTED] - LD
[REDACTED]s - VRMM

[REDACTED]

16th February 2023

Key

LD = Licensing Division
VRMM = Vigilance & Risk Management of Medicines
NIBSC = National Institute for Biological Standards & Control
Comms = MHRA Communications
IE&S = Inspection, Enforcement & Standards

¹ joined during item 6

² joined during item 2

³ presented item 2

⁴ supported specific items

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 Breuer, Goldblatt & Sir Michael Jacobs for this meeting.

1.5 The Chair welcomed the following invited experts for their specific items:

[Redacted]
[Redacted] Public Health England

[Redacted]
NHS England [Redacted]
[Redacted]
[Redacted]
[Redacted]

[Redacted]
[Redacted] Cambridge University Hospital NHS
foundation Trust

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

[Redacted]
[Redacted]
[Redacted]
[Redacted]
UKHSA

[Redacted]
[Redacted]
[Redacted] NHS England & Improvement

- 1.6 The Chair welcomed the following observers to the meeting:

[REDACTED]
[REDACTED]
Public Health Scotland

[REDACTED]
[REDACTED] Public Health Wales

Professor Wei Shen Lim
Chair of JCVI

2. UKHSA/NHSE presentations on anaphylaxis

- 2.1 The EWG heard presentations from UKHSA and NHS England on anaphylaxis and COVID-19 vaccines. These included an assessment of anaphylaxis emergency care presentations on the day of COVID-19 vaccination ‘pre’ and ‘post’ removal of the 15-minute wait time for mRNA COVID-19 vaccines following vaccination which found no significant increase in the rate of presentations after this change.

- 2.2 An analysis of reported incidents from vaccination sites and all health services was also presented including data from the Strategic Executive Information System (StEIS) compulsory reporting system for serious incidents and the National Reporting and Learning System (NRLS) optional incident reporting system. This analysis did not identify any episodes of analysis reported outside vaccination centres and no serious red flags were identified up to the data lock point of 15/11/2022. Direct reporting to the National COVID Incident Centre and data from Vaccination Point of Care systems also did not highlight any incidents of concern relating to the 15-minute wait up to the same time point. Similarly, qualitative data from ambulance services and a local vaccine service site visit, did not identify any safety issues with the suspension of the wait although these data had some limitations.

- 2.3 The EWG also heard feedback from a poll of members of the British Society for Allergy & Clinical Immunology (BSACI) expert group on dealing with allergic reactions to COVID-19 vaccines regarding their experiences of the removal of the 15-minute wait. None of the clinicians surveyed reported that, in their experience, this change had had an adverse impact on patient safety. The EWG were also informed that allergists were receiving referrals of people who had been turned away from COVID-19 vaccine clinics unnecessarily and heard a proposal for a risk-based approach for a 15-minute observation period in some high-risk individuals.

3. Review of anaphylaxis reports with mRNA COVID-19 vaccines

- 3.1 The EWG was provided with an overview of previous discussions of the temporary suspension of the 15-minute observation time in place for the mRNA COVID-19 vaccines which was previously discussed by the EWG on 14 December 2021, 13 January 2022 and 19 January 2022.

- 3.2 The EWG were presented with a summary of the Yellow Card reporting of anaphylaxis since the introduction of the temporary suspension. There have been no significant increases in reports of anaphylaxis since the suspension of the observation time, and with accumulating experience it was noted that there is a higher proportion of events reported following heterologous exposure with second and third doses which is expected on initial exposure to a different vaccine. The EWG was informed that there had been no new fatal

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reports since the suspension, and no strong trends of these events in those with multiple prior allergies.

- 3.3** The EWG were presented with data that had been provided by the Welsh, Scottish and Northern Irish public health authorities, none of which had identified increases in ambulance calls since the suspension or relaxation of the observation time, which indicated there had been no increase in anaphylaxis events that had not had prompt treatment. International data from Ireland where the observation time had also been suspended through public health policy had also not identified any concerns in their monitoring of anaphylaxis events post-vaccination.
- 3.4** The UK Health Security Agency (UKHSA) advice in COVID-19 Green Book chapter was discussed, with invited observers and presenters from NHS England and UKHSA explaining the current risk-based approach to the observation time, and that advice was in place to support those vaccinating individuals with prior allergic reactions to COVID-19 vaccine or other allergens.
- 3.5** The EWG considered the Yellow Card data to be reassuring, as was data provided by the public health bodies and from Ireland. The EWG supported maintaining the suspension in those 12 years and over for all authorised COVID-19 vaccines and for all doses based on the cumulative data, maintaining the risk-based approach detailed in the Green Book. It was recommended that the advice in the Green Book could be clarified and improved which UKHSA agreed to consider.
- 3.6** The EWG noted that this will remain as a public health policy rather than a regulatory change in the product information for the COVID-19 vaccines. The EWG recommended that anaphylaxis following COVID-19 vaccination remain under monitoring by the MHRA as an important safety concern.
- 3.7** The EWG discussed whether the permanent suspension should apply to vaccination of those 5-11 years old; it was concluded that while the body of evidence indicated the risk was very low in this age group, that this would remain a temporary suspension under review by the MHRA and the EWG and should be brought back to the EWG for discussion once further experience in the UK had accumulated.

4. Myo/pericarditis update for COVID-19 vaccines

- 4.1** The EWG were presented with an update on the Yellow Card reports for myocarditis and pericarditis with the three COVID-19 vaccines in use in the UK vaccination programme as well as new international data and literature.
- 4.2** The EWG were presented reporting rates for third/booster doses for the first time, with the EWG noting that the reporting rates for Pfizer/BioNTech and Moderna were lower than those seen for the primary dose schedule of the vaccines and that the rates were similar for both vaccines. The EWG were reassured by the lower reporting rates and considered that it would be useful to understand what factors may have resulted in the lower rates, such as potentially the half-dose for the Moderna booster and the different intervals between booster and primary series doses. For AstraZeneca, the reporting rates for first and second doses have remained similar to previous reviews and overall were lower than both of the mRNA vaccines.
- 4.3** The EWG were presented with long-term follow-up myocarditis and pericarditis reports to the Yellow Card scheme. The EWG heard that the majority of patients had recovered or were recovering from myocarditis and pericarditis at 3 months post-diagnosis and that

patients who had further diagnostic tests including cardiac MRI and ECG were not showing long-term complications associated with severe outcomes from myocarditis and pericarditis. Updated long-term follow-up from the US CDC also continued to show that the majority of patients recovered with no signs of serious long-term harm. The EWG were reassured by the follow-up data but agreed that this should continue to be monitored.

4.4 The EWG were informed of a signal of toxicity in overdose for colchicine that had been identified during routine signal detection, with 3 Yellow Card reports of overdose in 2021, including 2 fatal reports in children. The EWG noted comments from an expert cardiologist that colchicine is commonly used off-label for the treatment of pericarditis but is very rarely used in children. The EWG were reassured that none of the reports related to treatment of myocarditis or pericarditis and that Yellow Card data suggested use of colchicine for myocarditis and pericarditis was in line with current clinical guidance.

4.5 The EWG were presented with literature on reporting rates of myocarditis from the US and Israel. The EWG noted that the pattern of reporting remained consistent, with higher rates in young adult males after the second dose. In adolescent age groups, the EWG noted a similar trend for higher rates in males after the second dose.

4.6 The EWG concluded that the benefits continued to exceed the risks overall for all vaccines and for all authorised subpopulations. No regulatory action was required based on the data presented.

5. ONS / OHID data exploring the excess mortality seen in young males

5.1 The EWG were advised that data were anticipated to be published by the Office for National Statistics (ONS) and the Office for Health Improvement and Disparities (OHID) shortly exploring the excess mortality seen in death registration surveillance data in young males in 2021.

5.2 The EWG were reminded of data presented to them in December 2021 exploring the risk of cardiorespiratory related death following COVID-9 vaccination. Accepting that there were limitations to the data at that time, it was agreed that that study had not suggested an increased risk of cardiorespiratory death following vaccination with either the AstraZeneca or Pfizer vaccines.

5.3 The EWG noted that the evidence derived by ONS/OHID from linked death registration and vaccination data, and from cause of death data, was expected to show that there was no pattern of increased mortality in the weeks following vaccination compared to later time points and that the excess in mortality observed in the surveillance data was driven by increases in deaths due to external causes, including homicide and suicide.

5.4 The EWG were reassured by this update.

6. Valneva Vaccine

6.1 The EWG was presented with the rolling review for Valneva; the dossier is now at the second stage of assessment. [REDACTED]

6.2 [REDACTED]. The Chair mentioned that a further discussion on the Quality package will occur at a future meeting of the EWG.

6.3 The non-clinical review was not completed prior to the meeting: therefore, the EWG will review this in detail in due course at a future meeting of the EWG.

6.4 [REDACTED]

6.5 [REDACTED]

6.6 [REDACTED]

6.7 [REDACTED]

6.8 [REDACTED]

6.9 In closing, the EWG noted that it would be premature to make an overall decision on the COVID-19 vaccine Valneva.

7. Minutes of the COVID-19 VBR EWG meetings (Drafts)

- 01. Tuesday 23 March 2021
- 02. Wednesday 24 March 2021
- 03. Wednesday 31 March 2021
- 04. Tuesday 06 April 2021
- 05. Monday 19 April 2021
- 06. Monday 26 April 2021
- 07. Tuesday 04 May 2021
- 08. Friday 07 May 2021
- 09. Monday 10 May 2021
- 10. Monday 17 May 2021
- 11. Monday 24 May 2021

12. Tuesday 25 May 2021
13. Tuesday 01 June 2021
14. Monday 07 June 2021
15. Monday 14 June 2021
16. Monday 28 June 2021
17. Friday 23 July 2021

7.1 All minutes listed above were approved as a true and accurate record of the proceedings, subject to amendments and queries which have been resolved to meetings where required and the recognition of Public Health England now called the UK Health Security Agency (UKHSA).

8. **Any Other Business**

None.

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

The next meeting has been scheduled for **Friday 18th February 2022 at 11:30.**

The Meeting today started at 11:32 and ended at

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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

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 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 Lachmann – Other relevant interest as a volunteer participant in the Oxford vaccine study and no other involvement in the study.

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.

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).

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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).

Dr Riordan - Other relevant interests - Participant in Oxford University's ChAdOx1 nCoV-19 clinical trial –received immunisation 27/8/2020. NPNS - Postgraduate External Examiner for Oxford University (Postgraduate Diploma in Paediatric Infectious Diseases). Member of the independent Data Safety Monitoring Board for COV-BOOST trial.

Professor Solomon - Other relevant interests – Professor Solomon provides clinical care for patients with Covid-19; chaired the MRC/NIHR committee which awarded funding for development of the Oxford Vaccine.

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.

Professor Weir - NPNS - Imperial College and Other relevant interest arising from his department collaborates with Imperial College on a number of clinical trials.

Observer

██████████ - NPS – was part of an expert working group ██████████
██████████ to discuss strategies to improve
'vacceptance'. ██████████ has not received any form of payment or other remuneration
as described above but a paper is expected to be published.

Professor Wei Shen Lim - NPNS arises from the institution (Nottingham University Hospitals NHS Trust) where Professor Lim works has received unrestricted investigator-initiated research funding from Pfizer for an unrelated prospective population-based cohort study of pneumococcal pneumonia in which Professor Lim is the Chief Investigator.