

NOT FOR PUBLICATION

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

Minutes of the meeting held on **Tuesday 4th May 2021** at **14:00** via videoconference

Participants Present

Members

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

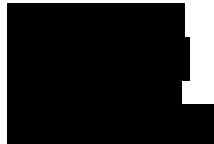
Apologies

- Professor J Breuer
- Professor K Hyrich
- Professor H J Lachmann
- Professor C Weir

Observers



Professor W S Lim



Secretariat



Professional Staff of MHRA Present

Principal Assessors

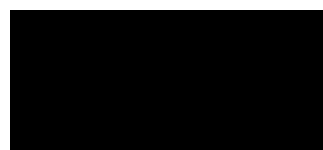
- Dr J Bonneriea - LD
- VRMM

Presenters supporting specific items

- VRMM
- VRMM
- VRMM
- Mr P Tregunno - VRMM

MHRA Observers

- VRMM
- LD
- VRMM
- LD
- Dr S Branch - VRMM
- MHRA-NIBSC
- MHRA-Policy
- VRMM
- Comms
- VRMM
- VRMM
- LD
- VRMM
- LD



4th February 2022

Key

- LD = Licensing Division
- VRMM = Vigilance & Risk Management of Medicines
- Comms = MHRA Communications
- NIBSC = National Institute for Biological Standards & Control

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, Hyrich, Lachmann and Weir for this meeting.

1.5 The Chair welcomed the following observers:

Mr [REDACTED]

Dr [REDACTED] Public Health England

Professor [REDACTED] JCVI

Dr [REDACTED] Public Health Agency

Dr [REDACTED]

Professor Wei Shen Lim
Chair of JCVI

Dr [REDACTED]
Public Health Scotland

Dr [REDACTED]
Public Health England

Dr [REDACTED]
[REDACTED] Public Health Wales

Dr [REDACTED]
[REDACTED]

- 2. Update on COVID-19 Vaccines and risk of thromboembolic events with concurrent thrombocytopenia**
- 2.1** The EWG was presented with the latest data on thromboembolic events with thrombocytopenia associated with the authorised COVID-19 Vaccines up to a data lock point of 28 April 2021. Summaries of the CDC/FDA and Health Canada reviews of thrombosis with thrombocytopenia syndrome associated with the Janssen COVID-19 vaccine were also presented. The data lock point for the Janssen vaccine was 12 April 2021.
- 2.2** A review of recent publications concerning the AstraZeneca COVID-19 vaccine identified a paper on a proposed mechanism, a study reporting the prevalence of anti-PF4 antibodies in Norwegian health care workers, 2 small case series and 3 case reports. The EWG noted that two patients in a [REDACTED] cases series experienced thrombotic events after receiving a 2-day course of intravenous immunoglobulin but 1 of these patients responded well to eculizumab.
- 2.3** The EWG was also presented with analyses of Yellow Cards reported up to the 21st April data lock point including analyses of numbers of reports by report date, by reaction date and by vaccination date. Charts were also presented showing the time between vaccination date and reporting date and days between fatal event dates and reporting dates.
- 2.4** An overview of the case reports associated with the AstraZeneca COVID-19 Vaccine was presented including a summary table of the 6 reported cases after a second dose. It was noted that none of the reported cases had cerebral venous sinus thromboses or platelet factor 4 antibodies.
- 2.5** The EWG was also given an overview of the platelet count distributions for venous and arterial thromboembolic events with thrombocytopenia. Half of those with reported platelet values and venous or arterial events had significant thrombocytopenia with platelet counts under $50 \times 10^9/L$, all of those with myocardial infarctions had counts under 50 whilst approximately 20% with deep vein thrombosis and/or pulmonary embolus had mild thrombocytopenia with counts of 100 or more.
- 2.6** The UK and foreign cases associated with the Pfizer, Moderna and Janssen COVID-19 vaccines were summarised using the same case definition.
- 2.7** The estimated number of second AstraZeneca COVID-19 vaccine doses administered has significantly increased to 5.9 million whilst the number of first doses has increased slightly, in line with the current deployment programme to 22.6 million. Estimated case incidence rates for CVST and CVST plus non-CVST events were presented by age-stratified 10-year intervals and by gender. The overall incidence rate is 10.5 (9.2, 11.9) per million for first/unknown doses and the overall fatal incidence rate is 2.1 (1.6, 1.8) per million doses. The estimated case incidence rate following a second dose is 1 per million doses. The risk estimates were then compared with the expected benefits of vaccine in age subgroups. The reported incidence rates are now plateauing, consistent with complete reporting of retrospective cases, so the estimated case incidence rates can be considered reliable.

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2.8 The EWG considered the following 3 questions:

2.8.1 **Question 1: based on the evidence presented does the EWG consider the benefit-risk balance remains favourable for all patients and for all age groups?**

The EWG advised that the overall benefit-risk profile of the AstraZeneca COVID-19 Vaccine remains positive. However, the benefits of immunisation in individuals aged under 30 years may be outweighed by the potential risks, depending on the status of the COVID-19 pandemic, its severity and impact on hospitalisation.

2.8.2 **Question 2: Does the EWG consider there might be an increased risk for the second dose of the vaccine?**

The EWG advised that the emerging data on the risk of thromboembolic events occurring with thrombocytopenia following second doses is reassuring but limited, and so the MHRA should continue to monitor second dose cases closely.

2.8.3 **Question 3: Does the EWG consider there is any need for action with regards to the Pfizer, Moderna or Janssen vaccines in relation to this potential risk?**

Based on available data, the risk associated with the Pfizer and Moderna COVID-19 vaccines appears lower than that associated with the AstraZeneca COVID-19 Vaccine. This risk should be continuously monitored and there is currently no need for further regulatory action.

2.9 In conclusion, the EWG did not identify any potential trigger for regulatory action.

3. **Any Other Business**

None.

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

The next meeting is scheduled to take place on Friday 7^h May. Time to be confirmed.

The Meeting today started at 14:02 and ended at 15:01.

Members are reminded that the content of papers and proceeding of the meetings are to be treated as 'Official – sensitive commercial'. Members are also reminded that, in accordance with the 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 must also declare any other matter which could reasonably be perceived as affecting their impartiality. Detailed guidance is set out in the Code of Practice

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 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.

Sir Michael Jacobs - Other relevant interest - As part of the academic role at the Liverpool School of Tropical Medicine, Sir Michael is a member of the Study Management Team and antiviral drug prioritisation group for the AGILE proof of concept (phase I/II) platform study. Sir Michael is also part of the team that submits new antiviral compounds against SARS-CoV2 for consideration by NIHR for testing on this platform. No commercial or financial interest in the trial or any of the compounds, or any pharmaceutical or biotechnology company.

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).

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.

Observers

Professor [REDACTED]

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.

Dr [REDACTED]

Dr [REDACTED]