

NOT FOR PUBLICATION

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

Minutes of the meeting held on **Monday 19<sup>th</sup> April 2021** at **17:15** via videoconference

**Participants Present**

**Members**

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

**Apologies**

Professor G Dougan  
Professor C Robertson  
Professor C Weir

**Observers**

[REDACTED]  
[REDACTED]  
[REDACTED]  
Professor W S Lim  
[REDACTED]  
[REDACTED]

**Secretariat**

[REDACTED]  
[REDACTED]

**Professional Staff of MHRA Present**

**Principal Assessors**

Dr J Bonneriea - LD  
[REDACTED]

**Presenter supporting specific item**

[REDACTED] - VRMM  
[REDACTED] - VRMM  
[REDACTED] VRMM

**MHRA Observers**

[REDACTED] - VRMM  
[REDACTED] - LD  
[REDACTED] - VRMM  
[REDACTED] - LD  
[REDACTED] - Comms  
Dr S Branch - VRMM  
[REDACTED] - LD  
[REDACTED] - MHRA-NIBSC  
[REDACTED] - MHRA-Policy  
[REDACTED] - VRMM  
[REDACTED] - VRMM  
[REDACTED] - VRMM  
Dr SP Lam - LD  
[REDACTED] - VRMM  
[REDACTED] - VRMM  
[REDACTED] - LD  
Ms N Rose - MHRA-NIBSC  
[REDACTED] - LD  
[REDACTED] - LD  
Dr K Wydenbach - LD  
[REDACTED]

4<sup>th</sup> 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 Dougan, Robertson and Weir for this meeting.

**1.5** The Chair welcomed the following observers:

**Mr** [REDACTED]

**Dr** [REDACTED] Public Health England

**Professor** [REDACTED]

**Professor Wei Shen Lim**  
Chair of JCVI

**Dr** [REDACTED]

**Dr** [REDACTED]  
Public Health Scotland

**Dr** [REDACTED] Public Health Wales

**Dr** [REDACTED]  
National COVID-19 Vaccination Programme

**2. Update on COVID-19 Vaccines and risk of thromboembolic events with concurrent thrombocytopenia**

**2.1** The VBR 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 14 April 2021. The data lock point for the Janssen vaccine was 12 April 2021. A summary of regulatory actions taken by the MHRA, EMA and FDA since the last EWG meeting on 12 April 2021 was also presented.

**2.2** Recent published case series and a case of secondary immune thrombocytopenia following the AstraZeneca COVID-19 Vaccine were also presented.

**2.3** An overview of the case reports associated with the AstraZeneca COVID-19 Vaccine was presented along with a summary table of reported second dose cases. The result of PF4 antibody testing is awaited in one probable second dose case and 4 others were considered unlikely on the basis of medical co-morbidities. The overall fatality rate has decreased to 19%.

**2.4** The UK and foreign cases associated with the Pfizer, Moderna and Janssen COVID-19 vaccines were summarised using the same case definition. It was noted that PF4 antibodies were detected in a Janssen clinical trial case. The EWG recommended that all suspected cases associated with other COVID-19 vaccines should be tested for PF4 antibodies to further characterise the risk and potentially clarify any causal mechanism(s).

**2.5** The estimated number of second AstraZeneca COVID-19 vaccine doses administered has significantly increased to 2.3 million whilst the number of first doses has increased slightly, in line with the current deployment programme. Age-stratified estimated case incidence rates for CVST and CVST plus non-CVST events were presented. The incidence rate following a second dose, based on a single probable case, was 0.4 (0.01, 2.4) per million compared to an overall incidence rate of 7.9 (6.8, 9.2) per million for first/unknown doses. The overall CVST incidence for first/unknown doses has increased from 2.4 to 3.6 per million doses and that for CVST and non-CVST has increased from 4.9 to 8.0 per million doses, although the overall fatal incidence rate for CVST and non-CVST cases after the first/unknown dose has increased from 1.2 to 1.7 per million. This small increase in the fatality rate is not statistically significant. The risk estimates were then compared with the expected benefits of the vaccine in age subgroups.

**2.6** Proposed triggers for regulatory action were presented and the EWG considered the following 3 questions:

**2.6.1 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 is more equivocal and may begin to be outweighed by the potential risks should the incidence rate further increase, although the benefit risk was also considered dependent on the status of the COVID-19 pandemic, its severity and impact on hospitalisation. The EWG also advised that the benefit-risk ratio for those aged 30 – 39 remained positive, although this requires close attention given the apparent increased number of cases. However, the EWG considered that no further regulatory action was warranted at this stage.

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

The EWG advised that the estimated point estimate for the incidence of thromboembolic events with thrombocytopenia associated with the second dose is only based on a single patient. Many people receiving their second doses have not entered the known risk period or will still be in it, so an absence of cases provides little reassurance. Overall, there is insufficient information to conclude on the magnitude of any risk associated with the second dose. The MHRA should continue to monitor second dose cases closely.

**2.6.3 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 EWG concluded that the risk associated with the Pfizer and Moderna COVID-19 vaccines appears lower than that associated with the AstraZeneca COVID-19 Vaccine. The identification of a confirmed Janssen case raises concerns that the potential risk associated with this vaccine, also based on a viral vector, is similar, although only a small number of cases have been reported. The EWG will further consider the ongoing marketing authorisation procedure for the Janssen COVID-19 Vaccine at its next meeting on 23 April 2021.

**2.7** In conclusion, the EWG did not currently identify any potential trigger for urgent regulatory action.

**3. Any Other Business**

None.

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

The next meeting is scheduled to take place on Friday 23<sup>rd</sup> April at 14:00.

The Meeting today started at 17:17 and ended at 18:32.

**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.

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 3<sup>rd</sup> 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.

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

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**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).

**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]