

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

Minutes of the meeting held on **Wednesday 19th January 2022** at **13:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer
Professor G Dougan
Mr VI G Fenton-May
Professor N French
Professor D Goldblatt
Ms S Hunneyball
Professor K Hyrich¹
Professor H J Lachmann
Professor P J Lehner
Mr R Lowe¹
Dr S Misbah
Professor Y Perrie
Dr A Riordan¹
Professor C Robertson
Professor K M G Taylor
Dr R Thorpe
Professor M Turner
Professor S Walsh
Mrs M Wang
Professor C Weir

Apologies

Sir M Jacobs
Professor S Price
Professor T Solomon

Invited Experts²

[REDACTED]

Observers

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

Lawyers

[REDACTED]

Secretariate

[REDACTED]

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea – LD
[REDACTED] – VRMM³

Presenters supporting specific items³

[REDACTED] - VRMM

MHRA Observers

[REDACTED] - VRMM
[REDACTED] - VRMM
[REDACTED] - LD
Dr S Branch - VRMM
Dr A Cave – Chief Safety Officer
[REDACTED] - MHRA-Policy
[REDACTED]
[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] – Comms

[REDACTED]

23rd June 2022

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 2

² participated for item 3 only

³ 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 Price, Solomon & Sir Michael Jacobs for this meeting.

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

[Redacted]
[Redacted]
[Redacted] NHS Lothian

1.6 The Chair welcomed the following observers to the meeting:

[Redacted]
[Redacted]
[Redacted] Public Health England

[Redacted]
[Redacted] Public Health Scotland

[Redacted]
[Redacted] Public Health Wales

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

[Redacted]
Public Health England

2. Update on the Open Safely Study results

- 2.1** The EWG was presented with results of the Open Safely study on the potential association between COVID-19 vaccines (AstraZeneca vaccine, Pfizer/BioNTech, Moderna) and specific acute neurological adverse events, including Guillain Barre Syndrome (GBS), transverse myelitis (TM) and Bell's Palsy (BP). Primary Care data from >17 million patients in England linked to emergency care, hospital admission and mortality records were used to estimate incidence rates for each outcome in a specified time window. GBS and TM are currently included in the summary of product characteristics (SmPC) for the AZ vaccine.
- 2.2** The EWG was informed of the self-controlled case series design used for this study
- 2.3** The EWG discussed the study results, including an increased risk of GBS and BP post AZ vaccine which was highest in the 40-64 years age group. The authors found an increased risk of TM following BNT162b2 vaccination following sensitivity analysis in the 40-64 years age group, but no increased incidence for any other outcomes or age groups following this vaccine. This association disappeared following stratification by history and the group agreed that this was most likely a spurious finding. The EWG noted that there was no increased risk of BP following mRNA-1273 vaccine and there were too few outcomes of GBS and TM to investigate an association after this vaccine.
- 2.4** The EWG noted that no evidence of an increased risk of any outcome was identified following a second dose with either ChAdOx1 or BNT162b2 vaccine. Furthermore, a head-to-head comparison using ratio-of-ratios found that the increase in post-vaccination rate of GBS following ChAdOx1 compared to baseline was twice as high as that for BNT162b2 vaccine.
- 2.5** The EWG concluded that overall, the data provided no new information of the association between ChAdOx1 vaccination and acute neurological outcomes beyond the evidence already available. However, this issue should be kept under review.
- 2.6** The EWG recommended that no regulatory actions were required for either of the vaccines including AstraZeneca vaccine, Pfizer/BioNTech, Moderna following the data of the paper; however, the EWG supported an update of the UK weekly summary of Yellow Card reporting to reflect the current evidence with regards to Bell's Palsy.

3. Pfizer/BioNTech & Anaphylaxis in 5-11 year olds

- 3.1** The EWG were provided with a summary of the recent CHM and EWG discussions on the suspension of the 15-minute observation time for mRNA COVID-19 vaccines. At the most recent EWG review of this suspension on 13 January 2021, it was agreed that the suspension remained appropriate; however, a separate review was requested on the reporting of anaphylaxis in 5-11 year olds following vaccination with Pfizer/BioNTech COVID-19 vaccine, the preferred vaccine for those under 18 years in the UK.
- 3.2** The EWG were presented with a summary of the Yellow Card and international data relating to anaphylaxis following Pfizer/BioNTech vaccine in 5-11 year olds. There has been extremely limited exposure in this age group in the UK, and only 16 Yellow Card reports in this age group in total; none of which reported anaphylaxis.
- 3.3** International data from other regulators and the company data on anaphylaxis in 5-11 year olds with the Pfizer/BioNTech vaccine were also presented to the EWG; the majority of international experience came from the US where over 8 million doses had been administered in the age group. The EWG noted there was one fatal report of suspected anaphylaxis in 5-

NOT FOR PUBLICATION

11 year olds; however the case did not meet the Brighton Collaboration Criteria case definition, and the causality with vaccination was unclear.

- 3.4** The international data indicated that anaphylaxis was very rare in this age group, and lower reporting rates were observed compared to that in the overall population receiving the Pfizer/BioNTech vaccine; in the US this rate was 10-fold lower. While the majority of reports indicated hospitalisation or emergency medical care for anaphylaxis, it was considered that this likely represented the complexities in identifying and treating anaphylaxis in this age group, and the precautions taken.
- 3.5** The EWG discussed and noted the different approaches to administering the CHM advice on the 15 minute observation time in the devolved administrations, and that different approaches might apply to any advice on the observation time for 5-11 year olds too.
- 3.6** The invited experts and EWG members commented that the data showed that this remained a very rare event in 5-11 year olds and the reporting rates from the US were particularly reassuring, where the largest experience was in this age group.
- 3.7** It was highlighted by EWG members and the invited expert that there should be a cautious approach in this age group, and the EWG were informed by NHSE, UKHSA and devolved administrations that operationally, these vaccines would typically be administered by healthcare professionals trained in vaccinating children and advice was available for those considered higher risk of anaphylaxis such as those with a history of anaphylaxis, and these individuals would be observed. NHSE agreed to remain in contact with MHRA and raise any potential safety data they become aware of.
- 3.8** The EWG concluded that as the risk of anaphylaxis in 5-11 years following Pfizer/BioNTech was very low, the suspension of the observation time could also apply to this age group. The EWG highlighted that this suspension would remain under close review by the EWG and CHM as more data accumulates, including in those 5-11 years old.

4. Any Other Business

None.

5. Date and time of next meeting

The next meeting has been scheduled for **Friday 4th February 2022 at 11:30.**

The Meeting today started at 13:31 and ended at 15:04.

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 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 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).

NOT FOR PUBLICATION

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).

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.

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

■ ■■■■■ – 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.