

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

Minutes of the meeting held on **Thursday 13th January 2022** at **12:30** 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 H J Lachmann
Professor P J Lehner¹
Mr R Lowe¹
Dr S Misbah
Professor Y Perrie
Professor S Price²
Dr A Riordan
Professor C Robertson
Professor T Solomon
Professor K M G Taylor
Dr R Thorpe³
Professor S Walsh
Mrs M Wang
Professor C Weir

Apologies

Sir M Jacobs
Professor K Hyrich
Professor M Turner

Invited Experts

[REDACTED]⁴
[REDACTED]⁵
[REDACTED]
[REDACTED]

Observers

[REDACTED]
[REDACTED]
[REDACTED]

[REDACTED]

25th August 2022

Professional Staff of MHRA Present

Principal Assessors

[REDACTED] – LD
[REDACTED] – VRMM⁶

Presenters supporting specific items⁶

[REDACTED] – VRMM
[REDACTED] – VRMM
Dr N Rose - NIBSC

MHRA Observers

[REDACTED] – VRMM
Dr S Branch - VRMM
[REDACTED] - NIBSC
[REDACTED] - LD
[REDACTED] - VRMM
[REDACTED] - MHRA-Policy
[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] - VRMM
[REDACTED] - VRMM
Mr P Tregunno – VRMM
[REDACTED] - LD
[REDACTED] – Comms

Lawyers

[REDACTED]

Secretariats

[REDACTED]
[REDACTED]

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 left during item 5

² joined during item 2

³ left during item 3

⁴ participated for item 4 only

⁵ participated for item 3 only

⁶ 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 Hyrich, Turner & Sir Michael Jacobs for this meeting.

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

[REDACTED]
[REDACTED]
[REDACTED] Cambridge University Health Partners

[REDACTED]
[REDACTED]
[REDACTED] UCL

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED] UK Experimental Arthritis Treatment Centre for Children (Behcet’s and scleroderma workstreams)

[REDACTED]
[REDACTED]
[REDACTED] Bristol Heart Institute

1.6 The Chair welcomed the following observers to the meeting:

[REDACTED]
[REDACTED] Public Health Scotland

[REDACTED]
[REDACTED]
Public Health Agency

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

2. Review of Yellow Card reports of anaphylaxis with mRNA vaccines following suspension of the 15-minute observation time

- 2.1** The EWG were presented with a review of anaphylaxis reports following the Commission of Human Medicines (CHM) decision to implement a temporary suspension of the 15-minute observation period following administration of an mRNA COVID-19 vaccine.
- 2.2** The EWG were informed that reporting numbers of anaphylaxis had remained consistent for both the Pfizer/BioNTech and Moderna vaccines, despite the increase in the number of doses administered as part of the booster deployment. The majority of reports received since the temporary suspension have occurred in patients who received a heterologous booster, which is consistent with anaphylaxis events being more likely on a first exposure. The EWG noted that there was a higher proportion of reports with a history of prior allergy compared to previous reviews. However, it was reassuring that individuals with a history of allergies and anaphylaxis are still being observed as per the advice in the Green Book.
- 2.3** The EWG were informed that Ireland had taken similar action to suspend the 15-minute observation period for administration of booster doses, to enable a quicker rollout of vaccines due to the Omicron variant. Ireland had retained the observation period for primary doses and for patients with a history of anaphylaxis.
- 2.4** The EWG were presented with international data which showed reporting rates for the Pfizer/BioNTech vaccine were higher for the first dose compared to both the second dose and booster dose. The EWG noted that no signal of anaphylaxis had been identified in the US vaccine adverse event reporting system (VAERS) and vaccine safety datalink (VSD).
- 2.5** The EWG heard from NHS England that the ambulance service had not seen an increase in callouts for anaphylaxis following vaccination and that the temporary suspension of the observation time had allowed increased throughput at vaccination centres resulting in more people receiving their booster vaccine. The EWG concluded that the temporary suspension of the 15-minute observation period should be continued.
- 2.6** The EWG considered that while children were not expected to be at an increased risk of anaphylaxis compared to adults, a further review should be undertaken before a decision to suspend the observation period for the 5 to 11 years age group is made. The EWG noted that further international data on use in children would be available shortly.
- 2.7** The EWG considered that further data from NHS England and other public health bodies would be needed to support the decision on whether to either reintroduce the observation period or to move to a permanent suspension.

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- 3. Multisystem Inflammatory Syndrome in Children (MIS-C) and Adults (MIS- A) and the Pfizer COVID-19 vaccine**
 - 3.1** The EWG was presented with an update on the currently available evidence regarding multisystem inflammatory syndrome in children (MIS-C) and adults (MIS-A) following vaccination with the Pfizer COVID-19 vaccine. The available data included an update on the literature evidence and spontaneous reports received via the Yellow Card Scheme with a data lock point of 10th January 2022, as well as a Company review of this issue.
 - 3.2** The EWG heard that a targeted follow up questionnaire was being used to obtain additional information on all new Yellow Card reports received of MIS-C/A. The Group were informed that a limited number of additional reports of MIS-C (n=3) and no new reports of MIS-A had been received since the previous review of this issue in November 2021. The EWG heard that from the information provided, three of the four MIS-C reports received cumulatively were potentially confounded by COVID-19 infection and in the fourth report, the patient had been treated for suspected Group A streptococcal infection.
 - 3.3** The EWG also heard that following an updated review of the available evidence to 26 October 2021 (including an observed/expected analysis), Pfizer had concluded that the evidence did not support a causal association with MIS-C/A but had committed to continuing to monitor the risk and to use a new PRAC-approved data capture aid for follow up of all MIS-C/A reports. The EWG were also presented with evidence from a small French study suggesting that COVID-19 vaccination may be associated with a lower incidence of MIS-C in adolescents.
 - 3.4** The Group were reassured that there was no indication for a concern based on the updated evidence presented and that vaccination may actually reduce the risk of MIS-C/A.
 - 3.5** The EWG did not recommend any regulatory action based on the updated evidence.
- 4. Update of myocarditis and pericarditis following administration of Pfizer/BioNTech, Moderna and AstraZeneca 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 informed that the reporting rates remained similar between the first and second dose of the Pfizer/BioNTech vaccine and that the reporting rates for the under 18 age group remained lower than the 18-29 age group. The Moderna reporting rates remained similar to the last update, with higher reporting rates after the second dose in the younger age groups and higher reporting rates when compared to the Pfizer/BioNTech vaccine. For AstraZeneca, the reporting rate has remained similar to previous reviews and overall were lower than both of the mRNA vaccines.
 - 4.3** The EWG heard that the nature of the Yellow Card reports was similar to that previously presented for the vaccines, with higher proportions of reports in males and in younger age groups, with reports for the mRNA vaccines seen in younger age groups compared to the AstraZeneca vaccine. The EWG heard that the Pfizer/BioNTech booster reports was evenly split between homologous and heterologous reports, where there had previously been a higher proportion for homologous booster schedules.
 - 4.4** The EWG were presented with international data and literature on myocarditis and pericarditis after the administration of booster doses. The EWG were informed that based on CDC data,

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reporting rates for Pfizer/BioNTech and Moderna were lower for the booster doses compared to the primary schedule. The EWG were presented a paper on an updated analysis of the Edinburgh study, which indicated an increased risk of myocarditis for the Pfizer/BioNTech vaccine following a third dose. The study did not identify any myocarditis events following 3rd doses for Moderna or AstraZeneca, however there was limited usage of these vaccines in the study period.

- 4.5** The EWG were presented with a paper on the outcome of myocardial metabolic changes following recovery from COVID-19 infection, indicating that patients who had signs of myocardial inflammation on positron emission tomography (PET) showed improvement when followed-up at an average of 52 days. The EWG considered that the mechanism between myocarditis following COVID-19 infection and myocarditis after COVID-19 vaccination may be similar and this paper showed reassuring long-term outcomes for patients.
- 4.6** The EWG concluded that the benefits continued to exceed the risks overall for each vaccine and for all authorised subpopulations. No regulatory action was required based on the data presented.
- 4.7** The EWG considered that future updates should focus on reports following booster doses and reports in the under 18 years age group, following the expansion of second doses to 12-15 year olds and potential roll-out to 5-11 year olds. Future reviews will also cover data on long term outcomes of myocarditis and pericarditis.
- 5. Pfizer vaccine for children and testing aspects**
- 5.1** The EWG were presented with information on the independent batch testing of a tris-sucrose, lower-dose presentation of the Pfizer vaccine for use in 5-11 year old cohort. Current request is for NIBSC to test three batches which will be offered to a vulnerable cohort within this age group.
- 5.2** The request to test and certificate these batches was received at short notice and required implementation of an amended protocol for each test used, including the potency test – cell infectivity with a fluorescent antibody detection method (FACS). The first trial resulted in an out of specification result for the potency test.
- 5.3** The EWG were presented with data from the tests applied and an initial root-cause analysis for the sub-optimal performance. The EWG were presented with historical potency assay performance data from NIBSC. They heard that the manufacturer's data showed the batches met the potency specification in their laboratory. Data from other OMCLs are not available. Information from the company submission for process performance qualification batches of the Tris-sucrose vaccine presentation were also made available.
- 5.4** The EWG heard that the NIBSC experts concluded that an issue with the potency assay developed in December 2021 cannot be readily resolved to meet the deployment date for the three batches in question.
- 5.5** The EWG agreed that the data presented, along with the historical performance of the assay at NIBSC, allowed the group to apply a waiver to the batches enabling NIBSC to certificate in the absence of their own lab potency data, subject to input from an additional expert working group meeting and subsequent endorsement by CHM. This meets the benefit-risk for availability of the vaccine to the vulnerable cohort.

6. **Any Other Business**

None.

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

The next meeting has been scheduled for **Wednesday 19th January 2022 at 13:30.**

The Meeting today started at 12:30 and ended at 14:26.

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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

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 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.