

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

Minutes of the meeting held on **Friday 4th March 2022** at **14:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor G Dougan
Mr VI G Fenton-May
Professor D Goldblatt¹
Ms S Hunneyball
Professor K Hyrich
Professor P J Lehner
Dr S Misbah
Professor Y Perrie
Professor S Price
Dr A Riordan
Professor C Robertson²
Professor T Solomon
Professor K M G Taylor
Dr R Thorpe
Professor M Turner
Professor S Walsh
Professor C Weir

Apologies

Professor J Breuer
Professor N French
Sir M Jacobs
Professor H J Lachmann
Mr R Lowe
Mrs M Wang

Invited Experts

██████████³
██████████³
██████████⁴

Observers⁵

██████████
██████████
██████████

Secretariat

██████████
██████████

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea – LD
██████████ – VRMM

Presenters supporting specific items⁶

██████████ – VRMM
Dr S Hopper - LD

MHRA Observers

██████████ - LD
Dr S Branch - VRMM
██████████ - MHRA-Policy
██████████ - VRMM
██████████ - VRMM
██████████ - VRMM
██████████ - Comms
██████████ - VRMM
██████████ – Government Legal Team
██████████ - LD

████████████████████
23rd June 2022

¹ joined during item 3
² joined during item 4
³ participated for item 2
⁴ participated for item 3
⁵ joined for items 2 & 3
⁶ supported specific items

Key

LD = Licensing Division
VRMM = Vigilance & Risk Management of Medicines
Comms = MHRA Communications

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, French, Lachmann, Mr Lowe, Mrs Wang & Sir Michael Jacobs for this meeting.

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

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED] Thrombosis UK

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
Oxford University Hospitals NHS FT

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
University of Liverpool

1.6 The Chair welcomed the following observers to the meeting:

[REDACTED]
[REDACTED]
Public Health Scotland

[REDACTED]
[REDACTED] Public Health Wales

[REDACTED]
NHS England [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

2. AstraZeneca (AZ) COVID-19 Vaccine and thrombosis with thrombocytopenia (TTS) – review of current information

- 2.1 Two invited haematology experts attended the meeting.
- 2.2 The EWG was presented with an overview of incidence rates over time relating to TTS and AZ COVID-19 vaccine. The EWG was also presented with relevant new literature concerning this safety issue.
- 2.3 The EWG heard that incidence rates underwent only small changes since recommendations by the Joint Committee of Vaccination and Immunisation (JCVI) were made on 7th April and 7th May 2021. The incidence rate following first dose AZ vaccine had risen from 14.8 (13.3, 16.3) in early June 2021 to 15.6 (14.1, 17.2) in late February. Following second dose, the incidence rate changed from 1.7 (1.2, 2.3) to 2.0 (1.5, 2.7) over the same period.
- 2.4 The EWG heard that steeper increases in the number of spontaneous reports of suspected TTS during Q2/2021 was due to continued large AZ vaccine usage in the UK during this period and increased awareness amongst the healthcare professional community. The use of this vaccine in the UK slowed significantly in August 2021 in line with JCVI guidance on vaccine preference for under 40s; the time window in which TTS incidence rates stabilised while AZ usage was still high only a few weeks in duration, AZ usage began to slow considerably thereafter.
- 2.5 The EWG was presented with a summary of findings of recent observational studies which further inform on the risk of TTS at a population level.
- 2.6 The EWG agreed with the conclusion of the paper that the current product information adequately reflects current evidence.
- 2.7 The EWG further agreed that weekly TTS updates are no longer required in light of the minimal changes to the TTS risk incidences and low AZ usage.
- 2.8 One invited expert suggested that improvements could be made to the product information. The MHRA agreed to receive proposals for amendments.
- 2.9 It was noted that the AZ vaccine continues to see high usage in other parts of the world and lack of data on TTS from these regions was most likely due to under-ascertainment. It was considered whether world-wide data on TTS would possibly be useful when assessing the product information and that an attempt should be made to obtain further data in this respect.

3. Presentation from [REDACTED] - cellular immunity induced by the virus and vaccines

3.1 The EWG heard a presentation from [REDACTED] on cellular immunity induced by the virus and vaccines. The slides presented are shown at **Annex III** to the minutes.

4. Spikevax dispersion for injection (MODERNA BIOTECH SPAIN SL) PLGB 53720/0002 - 0082 variation to extend the indication to children aged 6 to 11 years – For Information

4.1 The EWG heard that a variation to extend the therapeutic indication to individuals 6 to 11 years has been submitted via the EC decision reliance procedure. The EWG heard that the supporting data are from study mRNA-1273-P204, an ongoing phase 2/3 randomised placebo-controlled observer-blind clinical trial in children aged 6 months to 11 years. A summary of the study design and results was presented. EWG heard that for the primary immunogenicity endpoints of 50% neutralising titres and sero-response rate, the results in children aged 6 to 11 years were compared with the results for an external cohort of adults aged 18 to 25 years. Non-inferiority was demonstrated according to pre-specified criteria. The study was underpowered to demonstrate vaccine efficacy in children aged 6 to 11 years as measured by the incidence of symptomatic COVID-19 starting 14 days post dose 2. However, there was a trend in favour of Spikevax.

4.2 The EWG heard that clinical safety data were available for nearly 3000 children aged 6 to 11 years exposed to at least one dose of Spikevax and followed up for at least 28 days post dose 2. Regarding reactogenicity, when compared to an external cohort of adults aged 18 to 25 years, the frequencies of local adverse reactions and fever were higher, and the frequencies of arthralgia/myalgia were lower. Overall, there was no meaningful difference in reactogenicity profile between children aged 6 to 11 years and adults aged 18 to 25 years. No grade 4 events were reported. Regarding unsolicited adverse events, the EWG heard that no new safety signals were detected. No adverse events of special interest, including myocarditis/pericarditis, multisystem inflammatory syndrome in children (MIS-C), autoimmune disease, immune thrombocytopenia, anaphylaxis or severe/serious hypersensitivity, were reported.

4.3 The EWG noted that the antibody levels in the 6 to 11 year old cohort were the same if not slightly higher than the levels seen in the 18 to 25 year old cohort, but that T cell response data are awaited. The proposed dose of 50 micrograms was relatively reactogenic in children aged 6 to 11 years, and particularly the frequency of fever was higher than that observed in the 18 to 25 year cohort. The EWG will be interested to see data on the immunogenicity and safety of the 25 microgram dose in a cohort of 300 children aged 6 to 11 years when that becomes available later this year. EWG noted that study P204 was not powered to detect myocarditis. Overall, the EWG agreed that the reliance variation was approvable.

4.4 The EWG also noted that section 6.3 of the SmPC document supporting this item was not in line with the current granted GB SmPC. Specifically, the chemical and physical in-use stability of the punctured vial should be 6 hours rather than 19 hours at [REDACTED]°C to [REDACTED]°C. The EWG heard that the SmPC document provided to illustrate the paediatric variation was the EU version, and that this variation will not alter section 6.3 of the current granted GB SmPC.

5. **Any Other Business**

None.

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

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

The Meeting today started at 14:31 and ended at 16:02.

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).

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 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. Other relevant interest in AstraZeneca arising from being part of a collaboration in which the epidemiology and therapeutic approaches to Vaccine associated Thrombosis-Thrombocytopenia (VITT).

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).

NOT FOR PUBLICATION

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.

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 (2020/21) with Havas Life Medicom conducting the initiative on behalf of Pfizer to discuss strategies to improve 'vacceptance'. Ms Falconer has not received any form of payment or other remuneration as described above but a paper is expected to be published.