COMMISSION ON HUMAN MEDICINES (CHM)

COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP

Minutes of the meeting held on **Tuesday 29th December 2020** at **09:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer
Professor G Dougan
Professor N French
Professor D Goldblatt
Ms S Hunneyball
Professor K Hyrich
Sir M Jacobs
Professor H J Lachmann
Professor P J Lehner
Dr S Misbah
Professor S Price
Dr A Riordan
Professor C Robertson
Professor T Solomon
Dr R Thorpe
Mrs M Wang
Professor C Weir

Apologies

Professor P Shah

Members of the CTBV Expert Advisory Group

Professor B K Park
Professor M Turner

Members of the CPS Expert Advisory Group

Mr VI G Fenton-May
Mr R Lowe
Professor Y Perrie
Professor K M G Taylor (Chair of CPS)
Dr S Walsh

Observer

Professor S Ralston (Chair of CHM)

Secretariat

[redacted]

Professional Staff of MHRA Present

Principal Assessors[1]

Dr J Bonnerjea - LD
[redacted] - LD

Supporting specific items[1]

[redacted] - VRMM
[redacted] - LD
[redacted] - LD

MHRA Observers

Dr S Atkinson - Directorate
Dr M Bailey - MHRA-NIBSC
[redacted] - LD
Dr S Branch - VRMM
[redacted] - LD
Dr P Bryan - VRMM
[redacted] - VRMM
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
Dr SP Lam - LD
[redacted] - VRMM
[redacted] - LD
Mr K McDonald - LD
[redacted] - MHRA Policy
Ms T Moore - IE&S
[redacted] - LD
[redacted] - Government Legal Team
[redacted] - LD
Dr J Raine - MHRA CEO
Dr N Rose - MHRA-NIBSC
[redacted] - MHRA-NIBSC
[redacted] - LD
[redacted] – IE&S
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - VRMM

[1] supporting specifc items

Key
LD = Licensing Division
NIBSC = National Institute for Biological Standards & Control
VRMM = Vigilance & Risk Management of Medicines
CTBV = Clinical Trials, Biologicals & Vaccines EAG
CPS = Chemistry, Pharmacy & Standards EAG
CHM = Commission on Human Medicines
Directorate = Director of Operational Transformation
MHRA CEO = Chief Executive
IE&S = Inspection, Enforcement & Standards

[redacted]

18th January 2021

1. Introduction and Announcement

1.1 The Chair reminded Members 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 The following members, invited experts and observers declared interests and other relevant interests for this meeting:

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 joining 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 reference 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.

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 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.

Professor Weir - Other relevant interest arising from link to the Lothian NHS Board. NHS Lothian R&D has partially funded Professor Weir's post at University of Edinburgh, since 2010, so that he could provide methodological advice on health services research studies and clinical trials.

CTBV

Professor Park - NPNS in GSK Research & Development Ltd. and in Janssen as I received a research grant in the past two years. The grant has been handed over to a colleague in 2020 and the grant is due to finish in 2020. Professor Park received no direct payment. In addition, Professor Park have two active IMI grants for Transbioline and Quantitatve Systems Toxicology, he is the PI on the TransBioline grant for the University of Liverpool. Both grants are paid directly to the University of Liverpool.

Professor Turner – NPNS interest. Professor Turner is a Non Executive Director (non-remunerated) on the Board of the Cell and Gene Therapy Catapult (CGT).
CGT have been tasked by UK Government with re-purposing a factory in Braintree to manufacture either a vaccine or a therapeutic mAb. No decision has been made as to whether or what product CGT Braintree may be asked to manufacture and that decision will be made by UK Government. Professor Turner does not believe that CGT Board will have any material input into the decision as to what product may be manufactured.

CPS

Mr V'lain Fenton-May – None

Mr Robert Lowe – None

Professor Yvonne 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 Kevin Taylor – None

Dr Susannah Walsh – None

Observer – Chair of CHM

Professor Ralston – NPNS – Sanofi, Pfizer, Janssen, AstraZeneca & Other relevant interests in NHS Lothian and Oxford University. Professor Ralston has an honorary consultant contract with NHS Lothian but has not been involved in any trials relating to COVID-19. He also has agreed to be an external examiner for Oxford University clinical trials MSc; however, this has not yet started.

1.4 The Chair welcomed Invited Experts of the CTBV and CPS Expert Advisory Groups, and Observer, Professor Ralston, Chair of the Commission on Human Medicines (CHM)

1.5 Apologies were received from Professor Shah for this meeting.

2. AZ: Summary of safety review & AEs

2.1 The EWG heard a summary of the safety review and adverse events for AZD1222.

2.2 The EWG agreed, based on the data currently available, not to include hypersensitivity as an adverse drug reaction (ADR). The EWG agreed that those who experience hypersensitivity following a first dose of vaccine are contraindicated for the second dose as detailed in Section 4.3 of the SmPC. The EWG noted that systemic urticaria is considered a hypersensitivity reaction. The group agreed this should be made clear to those healthcare practitioners administering the vaccine via information in the green book. The EWG agreed that MHRA can raise with PHE the concern that systemic urticaria may not be understood to be a hypersensitivity reaction.

2.3 The EWG agreed that no specific precautions are required for the administration of the vaccine in individuals that have a clinical history of COVID-19 (+/- PCR confirmation) or in

those with no history of COVID-19 illness but a positive COVID-19 antibody test.. This is in line with the advice for the Pfizer/BioNTech vaccine.

3. AZ: Information for Healthcare Professionals and for Vaccine Recipient documents

3.1 The EWG heard a presentation on the Information for Healthcare Professionals for Vaccine Recipient documents.

3.2 The EWG discussed the statement that increasing the dosing interval increases efficacy of the vaccine in Section 5.1 of the SmPC. The EWG agreed to amend the wording to reflect the uncertainty around the exploratory analyses.

The EWG discussed how to encourage the timing of the second dose to 8 weeks rather than 4 weeks. The EWG considered whether to acknowledge the lower amount of data seen at the lower dosing interval (4 weeks).

The EWG discussed whether to include a general statement that protection following vaccine administration is not immediate.

The EWG agreed to delete the sentence 'In this subpopulation, efficacy has been inferred from immunogenicity data, see below.' from Section 5.1 of the SmPC.

The EWG noted the wording of the dosing interval needs to be consistent between the SmPC and the PIL. It was also questioned whether it should be mentioned in the product information that this information will be updated as more data becomes available.

The EWG heard that the QR code links to the equivalent of the SmPC and PIL and the adverse event reporting form.

3.3 The EWG noted the lack of information about the 7-day gap between COVID-19 vaccine and the flu vaccine in Section 2 of the PIL.

The EWG considered whether information about colds, i.e. that it is still fine to take the vaccine if you have a cold, should be included in the PIL. This had already been requested.

3.4 The EWG agreed that the proposed wording regarding neuroinflammatory disorders in section 4.4 of the HCP information should be moved to section 4.8. The EWG discussed how to include information about neuroinflammatory disorders in the PIL in lay terms. The EWG agreed to review the wording off-line.

3.5 The EWG agreed that the pregnancy/fertility/reproductive wording in the product information reflects the current non-clinical data.

4. AZ: Risk Management Plan

4.1 The EWG heard an update on the Risk Management Plan.

4.2 The EWG agreed to ask the company how they propose to evaluate patients taking immunosuppressant medications and individuals with primary immunodeficiency to demonstrate vaccine safety in this population. The EWG also noted patients with conditions such as inflammatory bowel disease and inflammatory skin disease would fall into these categories.

4.3 The EWG noted that individuals are given a vaccine card which holds the batch number of each vaccine and from this it will be possible to determine the immunogenicity of each batch an individual has taken.

4.4 The EWG discussed assessment of immunogenicity and how it varies from batch to batch and how PHE are assessing it, if they are. The EWG heard that MHRA have communicated with PHE with regard to the Pfizer/BioNTech vaccine and are awaiting a response. The EWG suggested this approach also be taken with the AZ vaccine.

The EWG agreed to recommend to CHM approval for use of the AZ vaccine under a Regulation 174.

5. Future Steps / Any Other Business

5.1 None.

6. Date and time of next meeting

Thursday 31st December 2020 at 10:30

The Meeting started at 09:31 and ended at 10:36

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Annex I

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.