COMMISSION ON HUMAN MEDICINES (CHM)

COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP

Minutes of the meeting held on **Tuesday 10th November 2020** at **14:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer
Professor G Dougan
Professor N French
Professor D Goldblatt[1]
Ms S Hunneyball
Professor K Hyrich
Sir M Jacobs
Professor H J Lachmann
Dr S Misbah
Dr A Riordan
Professor C Robertson
Professor P Shah
Professor T Solomon
Dr R Thorpe
Mrs M Wang
Professor C Weir

Invited Experts

Professor I J Douglas
[redacted]

Apologies

Professor P J Lehner

Secretariat

[redacted]

[1] Joined during item 3

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea - LD
[redacted] - LD

Supporting Specific Items

[redacted] - LD
[redacted] - LD
Dr P Bryan - VRMM
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD

MHRA Observers

Dr S Branch - VRMM
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
Dr SP Lam - LD
[redacted] - LD
Dr C Schneider - MHRA-NIBSC
[redacted] - LD
[redacted] - LD

Key
LD = Licensing Division
NIBSC = National Institute for Biological Standards & Control
VRMM = Vigilance & Risk Management of Medicines

[redacted]

18th November 2020

1. Introduction and Announcement

1.1 The Chair reminded Members that the papers and proceedings are confidential and should not be disclosed.

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 declared interests and other relevant interests to date:

Professor Sir Munir Pirmohamed - NPNS AstraZeneca - Research grant to UOL to support PhD in drug interactions. 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

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

Dr Misbah - NPNS - Holds honorary Senior Lectureship with University of Oxford & Oxford University Hospitals NHS Foundation Trust

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.

Invited Expert of the Covid-19 Vaccines Benefit Risk Expert Working Group declared the following interests:

Professor Douglas - Personal non-specific in Oxford University, lecturing fees in the last 12 months. Personal interest in GlaxoSmithKline – Shares, current holding Bayer – October 2019 fee for delivering investigator training related to Aflibercept. Non-personal in GlaxoSmithKline - current research grant
At the chair's discretion, Professor Douglas was permitted to remain for the discussion and to answer, but not ask, direct questions from the chair and other members.

[redacted] - Personal non-specific interest in AstraZeneca who provide [redacted] department at the London School of Hygiene and Tropical Medicine with an unrestricted research grant 2016-2021. The grant partially contributes to funding [redacted] salary. [redacted] research and employment is not dependent on this funding and Astra Zeneca have no influence on the nature of [redacted] research, or on reporting or dissemination of results**.** Other relevant interest as [redacted] is working on a statistical methodology paper and some of the co-authors are statisticians at Astra Zeneca in Cambridge. It's an academic paper on analysis of subgroups and neither I nor this work have anything to do with their business side (or any drugs at all).

The register of interests declared by participants had not been deemed to debar any other participation in line with the policy. No further interests were declared.

1.4 Apologies have been received from Professor Lehner for this meeting.

2. Minutes of the meeting held on Wednesday 28th October 2020

2.1 The minutes were approved as a true and accurate record of the proceedings, subject to the amendment of less abbreviations to specific paragraphs.

3. Plans for Vaccine Assessment for Nov/Dec – Verbal Update

3.1 The EWG heard a high-level summary update (via presentation) of the rolling assessments of the Pfizer/BioNTech mRNA vaccine (BNT162b2) and the AstraZeneca vaccine (AZD1222).

3.2 BNT162b2

3.2.1 The EWG heard that DHSC are working on a large communications piece and MHRA will contribute to that. MHRA informed if the vaccine is authorised, a Q & A will be prepared along with a public assessment report, and that MHRA would contribute to DHSC comms on 'myth busting'. The EWG agreed it would be useful for MHRA comms colleagues to be invited to the EWG to provide an overview of the communications plan.

3.2.2 The EWG heard that a separate CHM Expert Working Group has been in place since May to advise MHRA on its pharmacovigilance strategy. There are four strands to this: enhanced passive surveillance (yellow cards), targeted active surveillance (app-based), rapid cycle analysis and ecological analysis (based on electronic healthcare records) and epidemiological studies where required.

3.2.3 The EWG heard Dr Phil Bryan will give a short summary on these safety assessments at the next meeting.

3.2.4 The EWG heard that the MHRA have flagged to NHSEI that automated collection of vaccination records into electronic healthcare records is a key requirement for proactive surveillance.

3.2.5 The EWG discussed the issues surrounding the storage requirements of BNT162b2. The EWG heard the MHRA will be examining the stability data for the vaccine to see if it can support supply to the primary care sector.

3.2.6 The EWG heard the vaccine will have a median of 2 months safety data which is in line with FDA requirements regarding the safety exposure for an Emergency Use Authorisation of COVID-19 vaccines.

3.2.7 The EWG noted that the timings of the Pfizer interim analyses had been changed. It is expected that these changes were made when still blinded to the data to avoid bias and that the efficacy will be stated as 'unadjusted observed rate' and not 'adjusted observed rate'. This can be confirmed once the data has been received.

3.2.8 The EWG discussed the issues around releasing investigational medicinal product (IMP) for a mass vaccination programme. The company have referred to clinical trial

product, emergency use product and commercial product. It will not be clear which product is intended for the UK until MHRA receives the data.

3.2.9 The EWG heard that the company is seeking emergency authorisation in US. If MHRA can confirm that the product intended for the UK is the same as that for the US, this may provide some assurance.

3.2.10 The EWG heard a decision on the use of clinical trial product will likely be necessary in December.

3.2.11 The EWG discussed whether current placebo (saline) recipients will receive the trial product if it is known to be effective. The EWG heard that the company have not yet informed MHRA of their intentions however it was noted that FDA and WHO guidance recommends continuation with placebo control. The EWG discussed how in low income countries this could be their only opportunity to receive the vaccine.

3.2.12 The EWG discussed whether the safety of the lipid nanoparticles should be examined separately as the placebo is saline only. The EWG heard MHRA has already raised a non-clinical question on this and is awaiting a response from the company.

3.2.13 The EWG heard that if the double-blind trial is stopped this will mean only 2-3 months efficacy is available ahead of mass vaccination.

3.1.14 The EWG heard that WHO draft guidance on the minimum clinical criteria for [redacted] states a median of [redacted] months follow-up clinical data to be acceptable. It is noted that any real risks are usually observed within 6 weeks of the vaccination. Overall, the duration of follow-up for the trial is 2 years.

3.2.15 The EWG noted the independence of the MHRA in the decision-making process for the potential approval of the vaccine. It was also noted that the independence of the decision of the Vaccine Benefit Risk EWG and Commission of Human Medicines (CHM) is key. The EWG heard that MHRA has separated themselves from the vaccine taskforce in order to avoid any potential conflicts.

3.3 AZD1222

3.3.1 The EWG heard that recruitment to the AstraZeneca trial was near completion in the most recent communication a few weeks ago. The total number of participants will be lower than the BNT vaccine (around 20,000).

3.3.2 The EWG heard that AstraZeneca had planned interim analyses, but the statistical plan has undergone several revisions and MHRA have not seen the last version. The EWG heard that no clinical data has been provided to the MHRA yet. Quality (3 sequences) and non-clinical (1 sequence) data is under assessment.

4. <u>Any Other Business</u>

4.1 None.

5. Date and time of next meeting

The next meeting is scheduled to take place on **Tuesday 24th November 2020** at **2.30pm**.

Date and time of future meetings:

- **Monday 7th December (10.30am - 1pm)**
- **Tuesday 22nd December (11.30am - 2pm)**

The Meeting started at 14:31 and ended at 15:54.

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

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.