COMMISSION ON HUMAN MEDICINES (CHM)

COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP

Minutes of the meeting held on **Saturday 21st 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
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

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
Professor Y Perrie
Professor K M G Taylor (Chair of CPS)
Dr S Walsh

Observer

Professor S Ralston (Chair of CHM)

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea - LD
[redacted] - LD

MHRA Supporting specific items

[redacted] - LD
[redacted] - LD
Dr N Rose - MHRA-NIBSC
[redacted] - LD
[redacted] - LD

MHRA Observers

[redacted] - Government Legal Team
Dr S Atkinson - Dir
Dr M Bailey - MHRA-NIBSC
[redacted] - LD
[redacted] - LD
[redacted] - LD
Dr S Branch - VRMM
[redacted] - Accenture IT Support
[redacted] - LD
Dr P Bryan - VRMM
[redacted] - MHRA-NIBSC
[redacted] - VRMM
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
Dr SP Lam - LD
[redacted] - VRMM
[redacted] - LD
Mr K McDonald - LD
Ms T Moore - IE&S

Apologies

Professor P Shah

Mr R Lowe (Member of CPS)

NHS / PHE presenters for item 2

[redacted] – NHS Wales

[redacted] – NHS Northern Ireland

[redacted] – NHS England

[redacted] – NHS Wales

[redacted] – NHS England

[redacted] – NHS England

[redacted] – NHS England

[redacted] – NHS Scotland

[redacted] – PHE

[redacted] – NHS England

[redacted] - IE&S

Dr J Raine - MHRA CEO

[redacted] - LD

Dr C Schneider - MHRA-NIBSC

[redacted] - IE&S

[redacted] - LD

[redacted] - LD

Secretariat

[redacted]

[redacted]

[redacted]

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
NHS = National Health Service
PHE = Public Health England
IE&S = Inspection, Enforcement & Standards
Dir = Director of Operational Transformation
MHRA CEO = Chief Executive

[redacted]

7th December 2020

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.

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.

1.2 The following members declared non-personal interests and other relevant interests to date:

C19VBR EWG

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 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.

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 EAG

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. Certainly I don't believe that CGT Board will have any material input into the decision as to what product may be manufactured.

CPS EAG

Mr V'lain Fenton-May – 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

CHM (Observer)

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.

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.

The Chair welcomed

Members of the Clinical Trials, Biologicals and Vaccines Expert Advisory Group (CTBVEAG)

Chair and Members of the Chemistry, Pharmacy & Standards Expert Advisory Group (CPSEAG).

Chair of CHM – **Professor Ralston** who joined as an observer

NHS:

- [redacted] –Medical Director, NHS England

Public Health England (PHE)

- [redacted] – Deputy Director at PHE

NHS Deployment Team

- PHE **–** [redacted] (Paper – 201030 PHE Operating Model – central storage and UK distribution covid vaccine & products. Slides - Courageous UK supply chain)
- NHSE **–** [redacted] and [redacted] with [redacted] to assist.
- NHS Wales **–** [redacted] and [redacted]
- NHS Northern Ireland **–** [redacted]
- NHS Scotland **–** [redacted] **(**Paper – NHS Scotland CHM Covid-19VBR deployment)

2. The Expert Working Group (EWG) heard presentations on deployment from PHE, NHS England, NHS Wales, NHS NI and NHS Scotland

2.1 The EWG discussed whether whole populations should be vaccinated in rural areas due to difficulties in separating out vulnerable populations.

2.2 The EWG heard that packing down was noted as an option in order to reduce waste but seems to be problematic for all nations apart from Scotland.

2.3 The EWG heard from NHSE that wastage was estimated to be 15-20%. NHSW will adopt a zero-tolerance approach towards wastage but accepts due to the characteristics of the vaccine it will occur.

2.4 The EWG heard that information on the impact of shaking and movement of the vaccine during transit has been informally provided to NHS from Pfizer. The data needs to be submitted to MHRA first for review.

2.5 The EWG discussed the labelling of the diluent and questioned whether, as the diluent looks like the usual saline vial, the diluent for the vaccine will be colour coded to ensure the right diluent is used.

2.6 The EWG agreed that a series of SOPs are required from one end of the chain to the next in terms of processes and pharmaceutical oversight. Staff need to be adequately trained. Experienced vaccinators only may be used.

2.7 The EWG heard NHS confirm that a PPE distribution will be arranged to match the vaccination plan. Specific PPE is required at distribution sites to defrost the vaccine and has been set up.

2.8 The EWG heard 175 PILs are to be provided per pack. The PILs are currently in English language only but company are working to put them in different languages. It is not yet clear whether the patient will receive a PIL beforehand or at point of vaccination. The PIL will also be made available online.

2.9 The EWG noted the discussion around the possibility of distribution of the vaccine between end users in order to reduce wastage. The pack size limits flexibility and the characteristics of this vaccine may also be prohibitive to movement. Each site must commit to use an entire pack in the right time frame. Moving vaccine from one end-user would likely be acceptable only in extreme circumstances and in line with Regulation 174 to address lack of supply and its surplus.

2.10 The EWG agreed the cold chain will need to be validated in terms of temperature management and vaccine stability.

2.11 The EWG heard that it is usual practice to deliver to GPs in cold storage. GPs are requested to have the appropriate storage facilities (fridges) in order to qualify for vaccination and PHE are procuring fridges for GPs if they do not have adequate ones.

2.12 The EWG emphasised that collection of patient data in a timely manner is extremely important to gain knowledge on the safety of the vaccine as soon as possible during the mass vaccination campaign.

3. The EWG heard a presentation on the non-clinical assessment of BNT162b2

3.1 The EWG heard that responses to the 13 non-clinical questions posed to the company in October 2020 are awaited.

3.2 The EWG noted the lack of data on reproductive toxicity and histopathology and agreed the experts would review and discuss the available data with the non-clinical assessors. The EWG agreed to discuss it again at the next Vaccine BR EWG Tuesday 24th November 2020.

4. The EWG heard a presentation on the quality assessment of BNT162b2

4.1 The EWG heard there were no major quality objections. The EWG discussed the wide drug product specifications and heard that they are to be expected for the vaccine at this stage. Any results observed that seem out of line will be addressed.

4.2 The EWG noted the importance of measuring immunogenicity in patients in controlled trials once they have been vaccinated. Studies to validate the cold chain will also be important. If requested NIBSC could be involved in examining vaccine potency as it enters and leaves cold chain.

4.3 EWG heard that stability data are expected and that the company have been asked to provide information about shipment and impact of transporting defrosted product in the network and how the product is impacted by shear forces.

5. The EWG heard a presentation on the clinical assessment of BNT

5.1 The EWG discussed whether a limit should be imposed on the age of the population to receive the vaccine as the benefit risk balance is less clear in younger patients. However, it was noted that the setting may also be relevant to the benefit risk balance, i.e. healthcare practitioners. The safety data appears to be comparable between different age groups. The EWG heard that the company are yet to provide a breakdown of the numbers in each age group, but it is expected to be a good spread across. The EWG noted that the company proposed vaccination of subjects aged 16 and over.

5.2 The EWG discussed the vaccination of younger female healthcare practitioners of child-bearing age and whether it would be feasible for such women to undertake a pregnancy test with the roll out of vaccine. It may be the case that it is not necessary to withhold the vaccine from pregnant women but at this stage it is not clear due to the lack of clinical and non-clinical data.

5.3 The EWG noted that recommendations will be required regarding concomitant flu vaccination.

5.4 The EWG agreed that a decision will need to be made with some gaps in the data and it will be important this is communicated to the population at large.

6. <u>Date and time of next meeting</u>

Tuesday 24th November 2020 at 2.30pm

The Meeting started at 14:00 and ended at 17:06.

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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.