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

Minutes of the meeting held on **Monday 18th January 2021** at **10:30** 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
Dr S Misbah
Professor S Price
Dr A Riordan
Professor C Robertson
Professor P Shah
Professor T Solomon
Dr R Thorpe
Mrs M Wang
Professor C Weir

Apologies

Professor P J Lehner

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

PHE Representatives

[redacted]

COG-UK Representatives

[redacted]

Professional Staff of MHRA Present

Principal Assessors

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

MHRA Presenters supporting specific items[2]

[redacted] - LD

MHRA Observers

[redacted] - LD
Dr M Bailey - MHRA-NIBSC
[redacted] - VRMM
[redacted] - VRMM
[redacted] - MHRA-NIBSC
[redacted] - LD
Dr S Branch - VRMM
[redacted] - LD
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[redacted] - LD
[redacted] - LD - Medical Writer
[redacted] - VRMM
[redacted] - LD
[redacted] - LD
[redacted] - MHRA-NIBSC
Ms N Rose - MHRA-NIBSC
[redacted] - LD
[redacted] - IE&S
[redacted] - MHRA-NIBSC
[redacted] - LD
[redacted] - LD

[redacted]

24th March 2021

Secretariat

[redacted]

[1] Left after item 2
[2] Left after item 4
[3] supporting specific 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
PHE = Public Health England
COG-UK = COVID-19 Genomics UK Consortium
IE&S = Inspection, Enforcement & Standards
NIBSC = National Institute for Biological Standards & Control

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 and invited experts 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 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.

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 - NPNS - Imperial College and Other relevant interest arising from his department collaborates with Imperial College on a number of 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 Quantitative 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

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

1.5 The Chair welcomed [redacted] (Consultant epidemiologist) & [redacted] (Scientific Lead) from PHE. The Chair also welcomed [redacted] and [redacted] from COG-UK.

2. Presentation by PHE

2.1 Early assessment of COVID-19 vaccine effects using Pillar1 and 2 data

2.1.1 The EWG viewed slides and heard a presentation from PHE on the early assessment of COVID-19 vaccine effects using Pillar1 and Pillar 2 data.

2.1.2 The EWG questioned the possibility that individuals are becoming infected in vaccination centres themselves. PHE confirmed that in their enhanced surveillance they are adding questions around the vaccination visit in order to understand more.

2.1.3 The EWG noted it is concerning that the dynamics in first week post-vaccination follow what is known about infections with COVID-19.

2.1.4 PHE informed there are a group of people being tested as they developed symptoms post vaccination.

2.1.5 The EWG heard that in terms of comparison with data from other countries who also rolled vaccine out quickly such as Israel or the US, UK data may be consistent with Israel but more data is needed to make a comparison.

2.1.6 The EWG noted that in cases where those that have been vaccinated and show symptoms, there is a need to check carefully for virus escape. People who are asymptomatic can become carriers of the disease. It is particularly important to keep the asymptomatic under review in the elderly population. PHE informed that this may form part of what ONS are doing.

2.1.7 The EWG discussed the possibility that the apparent increase in risk of disease in the short time period immediately after vaccination could theoretically be due to an antibody sump which then dissipates when the vaccine takes effect.

2.1.8 The EWG heard that overall, these results are similar to those seen in Scotland, with the exception of the increase 2–3 days post vaccination.

2.1.9 The EWG noted concern about deaths observed in the few days after vaccination in care home residents and heard there are specific studies set up to look at these. The VIVALDI study will be used to look at this, but all care homes will be incorporated into an analysis.

2.1.10 The EWG heard that the initial group of data from PHE includes a significant number of people who have received their second dose at 21 days.

2.1.11 The EWG questioned whether there is increased testing in people who have had the vaccine by virtue of being symptomatic to the vaccine itself? PHE stated there is no dramatic rise but overall, the numbers tested do go up a little in the period 3-13 days post vaccination.

2.1.12 The EWG noted that some of these vaccines are quite novel and questioned whether after vaccination each individual might be expressing the antigen in body fluids and that vaccination could be giving false positives. The EWG noted that PCR tests involve multiple sites on virus but could theoretically capture vaccine mRNA depending on protocol used; however, it is unlikely the vaccine could be responsible for false positives.

2.1.13 The EWG heard that PHE does also hold information on lateral flow test results but these are not presented here.

2.1.14 The EWG found the data presented of great interest and looked forward to hearing more from future analyses.

2.2 Analysis of reinfections from the SIREN cohort

2.2.1 The EWG viewed slides and heard a presentation on interim analysis of the SIREN study.

2.2.2 The EWG heard that those who had symptoms had less severe symptoms from the initial review but PHE informed that this will be looked at in more detail going forward.

2.2.3 The EWG queried whether an inverse analysis had been performed on reinfections to evaluate whether the first infection was symptomatic or asymptomatic and see if it was linked to the second infection. PHE informed that they know all cases that were symptomatic in first infection; however, work still needs to be done with regard to asymptomatic infections.

2.2.4 The EWG noted that it is important to link with COG-UK and follow asymptomatic and symptomatic infections and questioned whether these cases are reinfections or re-emergence of original infection. PHE informed that this work is on-going and some may be reclassified at a later stage to ‘persistent’.

2.2.5 Results from interim analysis has all been done at hospital sites and is qualitative. PHE will carry out a quantitative analysis. PHE collect medical histories at enrolment.

3. Presentation by COG-UK

3.1 The EWG viewed slides and heard a presentation by COG-UK.

3.2 The EWG noted it is important to look at the genotype of the virus as demonstrated by COG-UK.

3.3 The EWG noted it is important to do forecasting and evaluate how to do it and how accurately it can be done. The significance of mutations is not known and the role of combinations or consolation of mutations as well as single mutations was discussed.

3.4 The EWG heard that COG-UK are ahead in terms of collating mutations but that there was a long way to go to translate that into what it really means for the future. Excellent surveillance methods are required to keep track of the incidence of severe disease and death and mechanisms to pick up people who are re-infected after vaccination or natural infections and mechanism to see if there is a surge in cases. The transmissibility with impairment to immunity will be most concerning.

3.5 The EWG discussed how vaccine companies get access to data and how to feedback from COG-UK and PHENO to discuss with the companies what they need if they should need to redesign their vaccines. The EWG heard much information is freely available on COG-UK website and COG-UK are happy to engage with companies but in an organised structured way. The EWG heard access to data in real time is important. MHRA will talk to vaccine companies this week and plan to discuss the regulatory approach to tweaking the vaccines. MHRA informed that a paper will come to EWG in the near future.

3.6 The EWG discussed the potential adaptation of coronavirus vaccines to mutations. We do not have an example of another virus where there is escape from the vaccine apart from flu which changes rapidly. The EWG heard that coronavirus mutates much more slowly than the flu virus. The number of transmissions drives the infection rate and what happens in people who are chronically infected. If transmission is stopped then that would reduce the likelihood of escape mutants.

4. Presentation on Agility Project

4.1 The EWG viewed slides and heard a presentation on the CEPI funded Agility Project.

4.2 The EWG heard that the Syrian hamster model was originally developed for SARS-2CoV as being an effective model for this virus and it is an appropriate model to look at vaccines.

4.3 The EWG that heard PHE have sufficient capacity to look at different antivirals and vaccines.

4.4 The EWG discussed the sources of convalescent plasma used. The EWG heard that PHE have eight sera supplied in large volumes from NIBSC sourced from blood transfusion service in the early part of outbreak (no later than summer). The EWG heard the sera used in this study is from healthy volunteers from blood transfusion service.

4.5 The EWG noted it would be interesting to look at virus as it moves back into animal system to see if counter-evolution occurs.

4.6 The EWG heard PHE are doing a [redacted] assay which is not technically intracellular but would be keen to talk about this off-line.

5. EWG discussion on *in vivo* adventitious agent testing for Covid-19 vaccine AZD1222

5.1 The EWG viewed slides and heard a presentation on *in vivo* adventitious agent testing for COVID-19 vaccine AZD1222.

5.2 The EWG had no particular concerns with removing *in vivo* adventitious agent testing for COVID-19 vaccine AZD1222. The EWG noted a test by test analysis may be required at some point.

5.3 The EWG discussed the use of intermittent metagenomics and agreed to ask the company if they are considering this approach for the future.

6. Review of Minutes

6.1 Wednesday 18th November 2020
Saturday 21st November 2020
Tuesday 24th November 2020
Friday 27th November 2020
Saturday 28th November 2020
Monday 7th December 2020
Thursday 10th December 2020
Thursday 17th December 2020
Tuesday 22nd December 2020
Thursday 24th December 2020
Tuesday 29th December 2020

6.1.1 The minutes listed above were approved as a true and accurate record of the proceedings, subject to some amendments to the relevant minutes.

7. Future Steps / Any Other Business

7.1 Members were reminded that:

The content of papers and proceeding of the meeting are strictly confidential and should not be disclosed.

All enquiries, approaches, interview requests and requests for comments made directly to you from the media or stakeholders, verbal or written, should be declined and referred to the agency's news centre in the first instance.

8. Date and time of next meeting

The next meeting is scheduled to take place on Friday 22nd January 2021 at 15:30

The Meeting today started at 10:31 and ended at 12:56

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