COMMISSION ON HUMAN MEDICINES (CHM)

COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP

Minutes of the meeting held on **Sunday 3rd January 2021** at **15:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor H J Lachmann
Professor P J Lehner
Dr S Misbah

Members of the CTBV Expert Advisory Group

Professor M Turner

Professional Staff of MHRA Present

Principal Assessor

Dr J Bonnerjea - LD

Presenters supporting specific items[1]

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

Secretariat

[redacted]

[1] supporting specific items

MHRA Observers

Dr S Atkinson - Directorate
Dr S Branch - VRMM
[redacted] – LD
Dr SP Lam - LD
[redacted] – Government Legal Team
[redacted] - MHRA-NIBSC
[redacted] - LD
Dr J Raine – MHRA CEO
[redacted] - LD
[redacted] - LD

[redacted]

19th July 2021

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
IE&S = Inspection, Enforcement & Standards

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 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.

CTBV

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 [redacted] to manufacture either a vaccine or a therapeutic mAb. No decision has been made as to whether or what product CGT [redacted] 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.

2. HLA Sensitisation Issue – MHRA and AZ Risk Assessments

2.1 The EWG was presented with a risk assessment of the potential signal of HLA sensitisation for recipients of the Covid-19 vaccine AstraZeneca which had been raised following cases of HLA sensitisation in subjects in a clinical trial of CMV vaccine.

2.2 The EWG noted the following points:

2.2.1 Covid19 vaccine AstraZeneca uses an adenovirus vector, which is non-enveloped. This is in contrast with the CMV virus vaccine which raised the signal (which uses a Lymphocytic Choriomeningitis Virus vector which is enveloped) and the other vaccine for which sensitisation has been reported which is HIV, also an enveloped virus. Therefore, host cell HLA is unlikely to be incorporated into Covid19 vaccine AstraZeneca virion particles as it would during the formation of an envelope during the budding off of an enveloped virion.

2.2.2 Details of the [redacted] performed by AstraZeneca to test a Covid19 vaccine AstraZeneca product batch for Host Cell Proteins and HLA did not find any HLA protein/peptides and the detection levels achieved were sufficiently sensitive.

2.2.3 Analysis of samples from 595 male subjects from Covid-19 vaccine AstraZeneca trials did not identify any sensitisation of vaccine recipients. All potentially HEK293 HLA-reactive antibodies detected in post vaccination samples were present in baseline samples taken prior to vaccination.

2.3 The EWG endorsed the findings of the risk assessment and considered that the available data does not present evidence of a risk and therefore should not be a barrier to transplant candidates and recipients receiving Covid-19 vaccine AstraZeneca.

2.4 The EWG made the following recommendations:

2.4.1 The EWG supported the proposal that AstraZeneca, as an additional pharmacovigilance measure, should conduct analysis of further samples from a larger proportion of trial participants, with comparison to samples from participants who received active control, on the basis of a valid statistical plan.

2.4.2 The EWG also supported the proposal that AstraZeneca, as additional pharmacovigilance, should perform LC-MS analysis of a small additional number of Covid19 vaccine AstraZeneca product batches. Further details should also be provided of the methods used for LC-MS including the relative sensitivities to detect membrane-bound and soluble proteins.

2.4.3 These additional pharmacovigilance measures should be performed as soon as possible and completed within a timescale to be determined by MHRA.

2.4.4 The EWG recommended that no update to the Covid19 vaccine AstraZeneca product information was required and that no proactive communications were required to patients and healthcare professionals.

2.5 The EWG reflected on the risks that Covid-19 infection poses to transplant candidates and recipients and the importance of their access to Covid-19 vaccination.

3. Future Steps / Any Other Business

None.

4. Date and time of next meeting

TBC

The Meeting started at 15:35 and ended at 16:22

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