COMMISSION ON HUMAN MEDICINES (CHM)

COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP

Minutes of the meeting held on **Thursday 31st December 2020** at **10:00** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer[1]
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
Dr R Thorpe
Mrs M Wang
Professor C Weir

Apologies

Professor P Shah
Professor T Solomon

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[1]
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[2]

Dr J Bonnerjea - LD
[redacted] - LD

Presenters supporting specific items

[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - Government Legal Team
Dr N Rose - MHRA-NIBSC
[redacted] - LD

MHRA Observers

Dr S Atkinson - Directorate
Dr M Bailey - MHRA-NIBSC
Dr S Branch - VRMM
[redacted] - MHRA-NIBSC
[redacted] - VRMM
[redacted] - VRMM
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - LD
Dr SP Lam - LD
Mr K McDonald - LD
[redacted] - MHRA Policy
Ms T Moore - IE&S
[redacted] - LD
[redacted] - LD
[redacted] - MHRA-NIBSC
[redacted] - LD
[redacted] - LD
[redacted] - LD
[redacted] - VRMM
[redacted] - LD

[1] joined during item 2
[2] 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
IE&S = Inspection, Enforcement & Standards

[redacted]

19th July 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 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 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

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 Professors Shah and Solomon for this meeting.

1.6 The EWG received the following message of thanks from [redacted], [redacted]

"Please pass on my thanks on behalf of the MHRA Board to all of the members of the Expert Committees, CHM and the Agency who have been involved in the decisions to approve two of the major, international COVID-19 vaccines before any other regulator in the world. I recognise that this has involved many hours of extra work, usually at short notice, right up to and over the Christmas period, so everyone should be rightly proud of their contribution to protecting public health and saving many lives as a result of this incredible achievement. Of course, the work does not stop here with the continuing demands on batch release, safety vigilance and security of the supply chain, as well as further analysis of new data on these and other new vaccines as they become available. However, this does feel like the "end of the beginning" as we work towards our common goal of beating this virus and that does feel like a good way to bring 2020 to a close and look forward to a brighter New Year".

2. Moderna Vaccine:

2.1 Legal aspects of Moderna Vaccine (mRNA-1273) decision

2.1.1 The EWG heard their discussion needs to cover a broader scope than was initially planned due to uncertainties over the particular batch to be supplied to the UK (an alternative batch may be available to that considered previously). The EWG were asked to shift their focus from a batch specific proposal to a conditional MA approval and the EWG was asked to consider the additional information required to ascertain if the vaccine meets the requirements for a Regulation 174 authorisation. The EWG were also asked to give specific consideration to the dosing interval.

2.2 Batch testing

2.2.1 The EWG heard the National Institute for Biological Standards and Control (NIBSC) very recently received the materials required to commence laboratory testing. Testing protocols at NIBSC are in development and some documentation is outstanding. The EWG heard that the novel tests will take more time to set-up. In the interim, to address independent control of batch/s being considered for temporary authorisation under Regulation 174 of the HMRs, the Austrian Official Medicines Control Laboratory (OMCL) has been contacted to discuss data sharing and/or testing on behalf of NIBSC.

2.3 Quality

2.3.1 The mRNA-1273 product development and initial production has been performed in the US, and manufacturing activities were subsequently expanded to sites in the EU. US sites will supply the US regions and countries proximal to the US; in a similar format, the EU sites will supply the EU/EEA and Great Britain. Data from a single commercial batch produced within the EU is available (drug substance (DS) site: [redacted]; drug product (DP) site: [redacted]

2.3.2 The EWG heard about the manufacturing process of the mRNA active substance and the lipid elements of the product. The dossier is structured with three drug substance sections (DS 1: mRNA, DS 2: SM-102 LNP, DS 3: mRNA-1273 LNP) and one drug product section (the lipid-nanoparticle (LNP) formulated mRNA-1273 vaccine filled into vials). The product includes one active substance i.e., the mRNA, although the Applicant had presented three drug substance sections; two of these should have been included in the drug product section and will need to be corrected when seeking a full marketing authorisation.

2.3.3 The EWG heard details of the manufacture of mRNA active substance, with the purified mRNA element of the drug substance stored in polyethylene storage bags at -15°C to -25°C (or forward processed without freezing), although there is currently limited data to support the proposed shelf-life.

2.3.4 The EWG heard about manufacture of the lipid nanoparticles (SM-102 LNP) including [redacted] The LNP dispersion is stored at -[redacted] C to [redacted]°C, supported by real-time stability data for 6 months for one batch.

2.3.5 The novel excipients (i.e. SM-102 and PEG 2000-DMG) used for the manufacture of the LNP without mRNA are different to those included in the other mRNA vaccine considered by the Commission. In the SM-102 LNP, the proportion of PEG 2000-DMG to SM-102 is relatively low.

2.3.6 The EWG heard mRNA-1273 LNP is stored in a buffer solution and long-term stability data ([redacted]°C to [redacted]°C) for one developmental batch (4 months) and one Phase I//II clinical batch (3 months) has been provided. Stability data was reassuring when stored at [redacted]°C to [redacted]°C.

2.3.7 There are some amendments required to the specifications for both the SM 102 LNP and mRNA-1273 LNP [redacted]

2.3.8 The EWG heard that the manufacture of drug product is [redacted] in a multiple dose vial (10 doses per vial), without preservative. Only one commercial batch at 60,000 – 70,000 vial scale has been produced in the EU [redacted] The EWG heard the batch manufactured in the EU was produced too recently to generate any stability data, and therefore US batch stability data is being used to support the shelf life claim. The applicant proposed a shelf life of 6 months at [redacted]°C, 30 days at [redacted]°C, an in-use (unopened product) time of up to 12 hours at [redacted]5°C. There were only limited stability data to date to support this.

2.3.9 The EWG heard the key outstanding issues from cycle 4 of the rolling review, after responses were received on 30-12-2020. The applicant has committed to provide DS and DP process validation data from the EU sites by 31 March 2021. Full comparability data for current commercial batches from EU sites to US material used in clinical trials is expected by 31 March 2021; these data will be required in order to confirm a full demonstration of comparability throughout product development. The EWG heard that the aseptic fill summary report has been provided and was deemed acceptable.

2.3.10 The EWG heard DS and DP release and shelf-life specification acceptance criteria are wider than justified by the batch data ([redacted]); only one batch is manufactured at the EU sites, reliance is placed on individual batch data from the EU sites. This will need to be clear in the conditions of the temporary authorisation under Regulation 174 of the HMR 2012. DS specifications are to be finalised, with more commercial scale experience, by 30 June 2021. [redacted]. The EWG heard that in relation to the PEG2000-DMG manufacturing process, a tightening of the specifications for both novel excipients have been requested.

2.3.11 [redacted]

2.3.12 [redacted]

[redacted]

2.3.13 [redacted]

2.3.14 [redacted].

2.3.15 The EWG discussed the bacterial challenge filter data and noted that the product is stated to be bactericidal without dilution. The MHRA informed the EWG that the reports provided indicate that proper controls for testing sterility of a bactericidal product are in place.

2.3.16 The applicant proposed to have different shelf-life assignments dependent on purity of drug product at release, but it is not acceptable for shelf life to be applied to batches individually, based on a calculated 50% purity at the point of vaccination.

2.3.17 The EWG heard that the assessment team consider the applicant's proposal for storage at [redacted]°C for up to 30 days at point-of-care site as a point of concern. The EWG considered the practical benefits for deployment, with storage at [redacted]°C after thawing the vials, to outweigh the risk of mRNA degradation. The MHRA also mentioned the spiking studies demonstrated that E. coli growth begins to increase at 12 hours, therefore a 12-hour shelf life once the vial is punctured is not appropriate. The EWG noted that an in-use shelf life of 6 hours after the vial has been punctured would also be consistent with the other COVID-19 vaccines. For an unpreserved product, the shelf life of the unopened vial (after removal from refrigerated conditions of 12 hours) could present a risk in terms of errors when understanding the different shelf lives, e.g. in terms of an unopened product being returned to refrigerated conditions. The EWG noted the odds of this occurring could be minimised by informative and clear labelling. The EWG also considered the benefits of a 12-hour unopened shelf life, in terms of distribution from central locations to remote areas. The MHRA informed the EWG that the current intention is to transport the product frozen. Once thawed the product could be more vulnerable to stress and shaking forces; further stability data has been requested to verify this. The request for stability data covers all modes of transport currently included in the deployment models, including data at [redacted]°C. The MHRA

added that for the product to be transported at room temperature, additional supportive data would need to be provided.

2.3.18 The EWG heard the GMP certification that was outstanding has now been provided.

2.3.19 The EWG noted issues suggest authorisation under Regulation 174 should be considered, rather than a Marketing Authorisation.

2.3.20 The EWG reached a consensus that issues were outstanding that require further data or further justification before a batch-specific release could be authorised; once these issues have been satisfactorily resolved a Regulation 174 authorisation could be considered.

2.4 Clinical

2.4.1 The EWG heard following vaccination with the first dose, VE is low for ~14 days, but after this period VE increases to ~94% (35 vs 2 cases) prior to the second dose. The regulation 174 letter requested specific guidance on whether, and to what extent, an extended interval between first and second doses can be allowed, giving operational flexibility and potentially allowing increased prioritisation of the first dose for as many people as possible. The EWG heard the primary analysis population (per protocol set) received the second dose 3-6 weeks after the first dose and there was very limited efficacy data for an interval greater than 6 weeks (~0.6% of participants). The majority of participants in the Pfizer/BioNTech (BNT162b2) trial received a 2nd dose close to or on day 21, though the range was also 3-6 weeks; whereas in the phase III trial of mRNA-1273 most participants received a second dose on day 29. In accordance with the product information for Pfizer/BioNTech (BNT162b2) the second dose is to be given at least 21 days after first dose. The product information for mRNA-1273 presently states the second dose is to be given one month after first dose, the EWG was asked to consider if this should be changed to, at least one month after first dose, or more precisely at least 28 days after first dose.

2.4.2 The Chair mentioned the indication and whether an interval at least 28 days apart was appropriate for mRNA 1273.

2.4.3 The EWG noted the data on Moderna vaccine support a dosing interval of at least 28 days and was reassured that immunologically it would be very unlikely that efficacy would drop substantially if the interval was to extend beyond 28 days.

2.4.4 The EWG asked for a breakdown of cases of COVID-19 occurring between the second dose and 14 days after the second dose to identify if the cases are occurring within the first 7 days, where protection could be attributed to the first dose, or the next 7 days, where the second dose could also be contributing to the efficacy seen. The MHRA informed the EWG that data breakdown by 7 days post second dose has been requested, though it should be noted that during the whole 14 day period cases were only seen on the placebo arm.

2.4.5 The EWG noted there is a disconnect between the immunogenicity data and the vaccine efficacy data. The increase in the neutralising antibody levels just prior to the second dose is ~5 fold, increasing shortly after the second dose to ~38 fold (spike-IgG binding). However, the correlates of protection are yet to be determined; the ~5 fold increase despite appearing comparatively low, may still be sufficient to drive the vaccine efficacy seen in post first dose data.

2.4.6 The Chair noted that post-vaccination effectiveness studies with 3-month interval data including those from academic groups e.g. SIREN, should be made available to the EWG. Once completed, the findings from these studies may help to inform the optimum interval

between doses for the other COVID-19 vaccines and to confirm if longer intervals provide sufficient vaccine efficacy in the real-world setting.

2.4.7 The EWG heard anaphylaxis has been upgraded from an important potential risk to an important identified risk due to a post-marketing case report of anaphylaxis. The risk minimisation measures include warnings about anaphylaxis; pharmacovigilance includes expedited reporting and follow-up of any cases. If the mRNA 1273 vaccine is authorised MHRA will be closely monitoring the post marketing data for anaphylaxis and hypersensitivity reactions in the same manner undertaken for the Pfizer/BioNTech vaccine.

2.4.8 The EWG heard use in patients with immunosuppression (missing information in the RMP) will be included in the long-term effectiveness study which will rely on a database from Kaiser Permanente (Southern California), but the study protocol is yet to be received. The EWG heard the other RMP issues are minor and do not preclude an authorisation.

2.4.9 The EWG noted it would be more helpful to a vaccinator to use product information wording on anaphylaxis used in Pfizer/BioNTech product information as it is more descriptive of the clinical features of anaphylaxis, hypersensitivity reactions and generalised urticaria. The CDC have unified advice on both mRNA vaccines (Pfizer and Moderna), therefore MHRA could also consider a common set of guidance.

2.4.10 The EWG noted the product information currently includes a statement to the effect of 'mRNA-1273 is not recommended for use for pregnant or breastfeeding women'. An amendment is required to reflect limited experience with use of the vaccine in pregnant women, and a recommendation that the vaccine is only used in this group following a benefit risk discussion with the potential recipient. The EWG advised inclusion of the following statement 'The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.' in section 5.3. The EWG also noted that the pregnancy registry will be an important form of post-marketing surveillance.

2.4.11 The imbalance in cases of facial palsy in the trial was noted and, therefore, facial palsy and how it presents, should be included in the product information on a precautionary basis notwithstanding the limited number of events. The EWG noted the importance of consistent use of lay language where applicable, across vaccines, and also that the symptoms are often more important to the lay reader who might not infer anything from the name of a medical condition alone. The MHRA informed the EWG that certain sections of the product information could be aligned with the text used for Pfizer/BioNTech.

2.4.12 The Chair noted the clinical issues are resolvable, but the quality issues require further data.

2.4.13 The EWG asked about when and how further data will be submitted to the UK post Brexit. The MHRA mentioned, when the company submit information to the EMA, they have been asked to provide the same information to the MHRA.

2.5 Viral Variants and the Moderna Vaccine

2.5.1 The EWG heard Moderna have provided to the MHRA a document that details their plans to evaluate the vaccine's efficacy against the SARS-CoV-2 viral variant first identified in Kent. The variant has 17 mutations in the viral genome, 8 of which encode parts of the spike protein. Moderna have tested animal sera and are intending to extend testing to sera from vaccinated human subjects, using functional testing in a [redacted] assay using a pseudovirus, developed to be a copy of the Kent viral variant. Moderna have already undertaken testing of mice and monkey sera with a number of variants that are closely homologous / share some of the same mutations as the Kent variant: these results suggest

that neutralising responses are similar to those produced when sera were challenged with the wildtype strain.

2.5.2 The EWG noted the laboratory data were encouraging, and noted that one of the variants tested, the mink sequence, includes a deletion which causes an S gene drop-out. The 501 mutation is of interest as it is responsible for increased virus-host receptor binding; it is beneficial that this sequence is included in the testing programme.

2.5.3 The EWG heard that PHE-Porton and NIBSC are coordinating to test new variants. The EWG noted the Genotype-Phenotype correlation aspect of COG-UK work could also serve as a useful resource.

2.5.4 The EWG noted that the multiple lineages of SARS-CoV-2 and continued testing of variants as they are identified, is key piece of work to be advanced forward. The EWG asked about the process to handle changes to the authorisations if the vaccines need to be modified in response to variants. The Chair informed the panel that this issue is due to be revisited.

3. Any Other Business

3.1 Oxford/AstraZeneca AZD1222 vaccine human leukocyte antigen (HLA) sensitisation to Human embryonic kidney 293 cells (HEK 293)

3.1.1 The EWG heard that NHS-BT have asked the MHRA if the AZD1222 vaccine could carry a risk of HLA sensitisation, and if there could be clinical consequences for patients on the transplant waiting list if they receive the vaccine. AZD1222 is developed using the HEK 293 cell line. The example of some clinical trial recipients of a cytomegalovirus (CMV) vaccine sensitised to HLA proteins mapped back to the HEK cell line was noted, although the data are limited. The EWG heard this is currently only a theoretical consideration for AZD1222, and any root-cause analysis has not yet been made available to MHRA. The letter asked the MHRA to confirm the absence of residual traces of HEK 293 cell components. As with any biological product derived from a cell line, levels of host cell proteins (HCPs) are well controlled (in each batch of AZD1222) but are not absent. AstraZeneca were provided with a copy of the NHS-BT letter and have informed the MHRA of their intention to urgently liaise with the medical director for the CMV vaccine trial to gain more knowledge about the cell line and HCP levels. AstraZeneca have also confirmed HLA antigens were not detected in AZD1222 batches, and further studies of the issue are planned.

3.1.2 The EWG heard currently available batch data shows the batches are well within HCP limits. However, the established limits approach used to inform these specifications is largely based on levels of HCPs from other vaccines, but of these vaccines only few use HEK cell lines.

3.1.3 The Chair asked the EWG if any urgent action is required given that the vaccine roll-out is starting 4th of January.

3.1.4 The EWG noted the approach that AstraZeneca have taken so far appears to be the correct one; spectrophotometry did not appear to show any HLA proteins. According to the batch data the levels of HCPs are very low, but it would be beneficial to compare the levels to historical CMV vaccine batch data. The EWG noted that a benefit-risk evaluation needs to be undertaken before deferring vaccination. The EWG noted that adenoviruses are non-enveloped, and therefore the scope to carry host proteins such as HLA antigens is highly limited. The EWG noted that more data are required including the sensitivity limits of the spectroscopy method.

3.1.5 The EWG noted that sensitisation is a potential serious previously unidentified risk and suggested alternative vaccines could possibly be used for those on the transplant waiting list. The Chair mentioned enabling patients to gain access to the Pfizer BioNTech vaccine may not be logistically feasible, because many of these patients cannot leave their homes and the cold chain needs to be maintained for this particular vaccine; availability may also be another caveat. The EWG heard that, in order to inform on the benefit-risk of the situation more accurately, the MHRA are rapidly seeking more data from the manufacturer of the CMV vaccine, as well as meeting with NHS-BT and AstraZeneca.

3.1.6 The EWG noted that patients with chronic renal failure are extremely vulnerable to COVID, and therefore extreme caution should be exercised when considering not to vaccinate this group.

4. Future Steps / Any Other Business

None.

5. Date and time of next meeting

Monday 4th January 2021 at 09:30

The Meeting started at 10:02 and ended at 12:57

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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.