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

Minutes of the meeting held on **Wednesday 31st March 2021** at **11:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer
Professor G Dougan[1]
Mr VI G Fenton-May
Professor N French[2]
Professor D Goldblatt
Ms S Hunneyball[3]
Professor K Hyrich
Sir M Jacobs
Professor H J Lachmann
Professor P J Lehner
Mr R Lowe
Dr S Misbah
Professor Y Perrie
Professor S Price
Dr A Riordan
Professor C Robertson
Professor T Solomon
Professor K M G Taylor
Dr R Thorpe
Professor M Turner
Dr S Walsh
Mrs M Wang
Professor C Weir

Apologies

Professor P Shah

Invited Experts

[redacted]

Observers

[redacted]

Professor W S Lim

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea - LD

Presenter supporting specific item

[redacted]

MHRA Observers

[redacted]
Dr S Branch - VRMM
[redacted]
Dr J Raine - MHRA CEO
Ms N Rose - MHRA-NIBSC
[redacted] - MHRA-NIBSC
[redacted]
Mr P Tregunno - VRMM

Secretariat

[redacted]

Key
LD = Licensing Division
NIBSC = National Institute for Biological Standards & Control
VRMM = Vigilance & Risk Management of Medicines
MHRA CEO = Chief Executive
Comms = MHRA Communications

[redacted]

[1] joined during item 3
[2] joined during item 2
[3] joined during item 5

4th February 2022

1. Introduction and Announcement

1.1 The Chair reminded Members, invited Experts and observers 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 Participants declared interests and other relevant interests for this meeting listed at **Annex II** to the minutes.

1.4 Apologies were received from Professor Shah for this meeting.

1.5 The Chair welcomed Invited Experts, Professor [redacted], Professor of [redacted] who presented item 2 and left after this item. Dr [redacted] Public Health England joined and presented item 6.

1.6 The Chair welcomed the following observers:

[redacted] – NHS England
[redacted] PHS
[redacted] – PHW
[redacted] Miller – PHE
[redacted] – NHS England
[redacted] – PHE
[redacted] – PHE
Professor Wei Shen Lim – JCVI

2. Vaccine Safety Study

2.1 The EWG viewed slides and heard a presentation by researchers at the University of Edinburgh on the studies conducted in Scotland using a nationwide platform called EAVE (early assessment of antivirals and vaccine effectiveness) II. EAVE II was originally created to respond to the N1H1 (swine flu) pandemic, and is used to link data to monitor, understand and mitigate the effects of a pandemic. The aim of EAVE II is to create a national, real-time prospective cohort, using Scotland's health data infrastructure to investigate the effectiveness and safety of vaccines and treatments.

2.2 The EWG heard that the objectives were i) to investigate the impact of the first dose of vaccine on COVID-19 hospitalisations, ii) to estimate the frequency and characterise severe COVID-19 events i.e.COVID-19 hospitalisations and deaths after 14 days post first dose, and iii) to investigate the association between first doses of vaccines and vascular adverse

events, specifically venous thromboembolic disease and cerebral sinus venous thrombosis (CSVT), haemorrhage, and thrombocytopenia and idiopathic thrombocytopenia (ITP).

2.3 The EWG heard that a prospective cohort study was conducted using the EAVE II database comprised of linked vaccination, primary care, real-time polymerase chain reaction (RT-PCR) testing, hospitalisation and mortality records of 5.4 million people in Scotland. A time-dependent Cox model and Poisson regression models were fitted to estimate effectiveness against COVID-19 related hospitalisation (defined as 1-adjusted Hazard Ratio) following the first dose of the Pfizer/BioNTech and AstraZeneca vaccines.

2.4 The EWG noted that the overall vaccine effect in relation to risk of hospitalisation was assessed across all age groups. The findings of the study for both vaccines showed reduced risk of hospitalisation amongst the vaccinated (with a vaccine effect of 70% at 21-34 days post-vaccination) compared to the unvaccinated individuals. It was noted that limited data was analysed for the AstraZeneca vaccine beyond 28 days post-vaccination, but the data showed some effect of a comparable order of magnitude to the clinical trials. The EWG also heard that the results of the vaccine effect were similar in those aged 80 years and over with a vaccine effect of 60-90%.

2.5 The EWG heard that the national data demonstrated correlation between a single dose of the Pfizer/BioNTech and AstraZeneca vaccines and reductions in the risk of COVID-19 related hospitalisations in Scotland.

2.6 The EWG heard the details of a second ongoing prospective cohort study which investigated the effect of Pfizer/BioNTech and AstraZeneca vaccines 14 days after the first dose to second dose or end of study. The analysis period was between 08 December 2020 to 08 March 2021.

2.7 The EWG heard that the results showed that out of 1,679,756 individuals that were given the first dose of either vaccines, 481 were hospitalised and 260 died of COVID-19. The EWG heard based on the data from distribution of incidents, the majority of deaths occurred with the Pfizer/BioNTech vaccine which was targeted to people in care homes, whereas the AstraZeneca vaccine was given to over 80 year olds who were largely living in the community.

2.8 The EWG heard the interim analysis based on adjusted rate ratios shows higher risk of severe outcomes (hospitalisation or death) in males (with 33% increase) and in the older population aged 80 and over. It was also noted that other characteristics such as presence of comorbidity, higher deprivation, smoking status and no previous COVID-19 infection also influenced the risk ratio of both vaccines.

2.9 The EWG was also presented with details of a third ongoing study to investigate the association between first doses of vaccines and vascular adverse events. The EWG noted that an incident case-control study nested within the prospective cohort study was undertaken on data from consultations requested during a period from 8 December 2020 to 14 March 2021. The EWG heard that very few CSVT events (16 cases) were reported, with less than 5 events amongst individuals vaccinated with the Pfizer/BioNTech or AstraZeneca vaccines. It was reported that most of the events were in unvaccinated individuals. The EWG noted that further analysis will be performed once more data is collected.

2.10 The EWG heard that a seasonal pattern was not associated with the number of consultations; however, an increase in the number of consultations for ITP was observed in 2021.

2.11 The EWG heard that the observed and expected number of events, post vaccination, in the incident case-control study showed no evidence of an increased risk of venous thromoboembolic disease (excluding CSVT), haemorrhage and thrombocytopenia. However, the observed number of ITP events in those vaccinated with AstraZeneca vaccine was higher compared to the expected number of events in those aged 60-79.

2.12 The EWG heard that the preliminary results suggested that there is a signal for ITP with 0.82 cases per 100,000 doses of vaccine. It was also noted that due to the lag of discharge of data, analysis may be incomplete as this is reliant only on the GP data. Further analysis will be carried out to investigate whether the ITP is the causal risk with the AstraZeneca vaccine.

2.13 Discussion/Comments

2.13.1 The EWG asked whether the 260 cases that died were confirmed COVID-19 deaths based on death certificate data. The investigator stated that the deaths mainly occurred in elderly patients who tested positive for COVID-19 and died within 28 days of contracting COVID-19. The association of deaths with COVID-19 was also confirmed from the death certificates.

2.13.2 The EWG questioned whether genomic sequencing of virus had been conducted on samples obtained from the 260 who had died and whether this data could be linked to different variants of concern. The investigator stated that work is in progress, whereby a systematic genome sequencing of the positive cases is conducted, and the potential vaccine failures are linked to the genome data in order to identify variants.

2.13.3 The EWG asked whether smoking was independent of the other risk factors such as comorbidity, sex and deprivation. The investigator stated that smoking was an independent factor.

2.13.4 The EWG enquired whether differences were seen in mortality between individuals admitted from care homes versus from the community, and whether an indication of exposure to higher viral load in care homes was seen which had contributed to hospitalisation and death. The EWG heard that initially there were difficulties obtaining the necessary data to explore this question, but recently this has changed, and the relevant research may soon be possible.

2.13.5 The EWG asked whether analysis of data after 21 days, where immunity appears, or 28 days post vaccination will be undertaken. The investigators confirmed that data analysis following 21 and 28 days post vaccination will be undertaken, and the results will be provided to the MHRA.

2.13.6 The EWG inquired if there was a correlation between obesity and death. The investigators confirmed correlation between obesity and death when presented as a single factor, however, obesity is dominated by the other factors when present with comorbidities.

2.13.7 The EWG noted that natural ITP events are more common in those aged 60 and over. However, data analysed confirmed that more events of ITP were observed than expected in those aged 60-79 with the AstraZeneca vaccine. It was not possible to compare the data for those aged 40 and under due to limitations of the dataset.

2.13.8 The EWG asked that if there is a possibility of tracking the ITP patients aged 60-79 years to confirm that the diagnosis was correct and measure the anti-PF4 antibody in those patients. The EWG heard that it is problematic to link data to these patient records as they are anonymised in line with the privacy agreements on GP data.

2.13.9 The EWG noted both ITP and heparin induced thrombocytopenia (HIT) syndrome are both autoimmune conditions affecting the platelets. However, in classic ITP the most commonly elevated antibodies against platelets are glycoprotein IIb-IIIa or Ib-IX, whereas in HIT syndrome antibodies against platelet factor 4 (PF4) are elevated. The EWG noted additional information is needed to understand the pathogenesis of ITP and HIT and to evaluate potential relationships between them. The EWG also noted that ITP is a complex diagnosis that can be difficult to validate.

2.13.10 The EWG asked if there was a possibility of the ITP cases were also previously diagnosed (prior to vaccination) and if the reduction in platelets was exacerbated rather than initiated by the vaccine. The investigators stated that a special permission is required to retrace these patients and perform further analysis. The EWG advised that these issues need further investigation as it is known that ITP can be affected by a precipitant. The possibility that the case reports reflect previously undiagnosed and/or subclinical clinical ITP also needs to be explored.

2.13.11 The EWG were informed by the MHRA that analysis on hospital episode statistics (HES) data were conducted to investigate the ecological analysis of ITP pre-pandemic and during the pandemic. The EWG heard that data from Public health England showed a marked reduction in ITP cases during the pandemic compared to pre-pandemic levels. CPRD continues to conduct sequential monitoring for ITP which identified an excess number of ITP cases with the AstraZeneca vaccine in younger patients. The MHRA noted the source of the large difference in the underlying baseline rate of ITP in previous years versus during the pandemic need to be investigated. The EWG noted it may be useful to undertake a self-control case series analysis of the CPRD data to mitigate against changes in baseline rates.

2.13.12 The EWG suggested that further analysis is required to confirm the ITP signal with the AstraZeneca vaccine.

3. Risk of anaphylaxis with Pfizer/BioNTech COVID-19 vaccine and review of the recommended observation time

3.1 The EWG noted that Pfizer/BioNTech COVID-19 vaccine UK product information (PI) currently advises that those with known hypersensitivity to any of the vaccines ingredients should not receive the vaccine, and that appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction. Close observation for at least 15 minutes is also recommended. This issue has been previously considered twice in January by the EWG when the current wording to the PI was endorsed. The EWG heard that the total number of doses administered for this vaccine to 24th March 2021 is 10.9 million first doses and 2.5 million second doses. The MHRA has received a total of 256 reporting PTs of anaphylaxis or the related terms (reporting rate of 1.9 cases per 100,000 doses) and among them 87 cases were identified as being possibly or probably meeting levels 1-3 diagnostic criteria of the Brighton collaboration criteria (reporting rate of 0.65 cases per 100,000 doses). Around 60% of anaphylaxis cases were reported to occur within 15 minutes after vaccination.

3.2 The EWG agreed that the current PI is appropriate and agreed on the need to keep the recommendation for 15 min observation time. Although better evidence on possible transmission occurring in vaccination centres is welcomed, it is at present difficult to attribute a possible increased risk of contracting Covid19 to the waiting time alone, without also considering all other steps involved in the vaccination process (for example travel to the vaccination centre on public transport). The EWG discussed the need to maintain public confidence in the program and the fact that a change in recommendations could generate confusion in the public and loss of confidence if supervision is withdrawn and an incident occurs.

4. Safety of COVID-19 Vaccines in Pregnancy

4.1 The EWG noted that limited information is available for use of COVID-19 vaccines in pregnancy and so are not currently recommended for use during pregnancy but may be given to front-line healthcare workers and pregnant women with underlying health conditions that place them at greater risk of severe illness.

4.2 Yellow card reports have been received for both the Pfizer-BioNTech and Oxford-AZ vaccines (n=89 and 114 respectively), with most reports related to vaccination occurring early in pregnancy.

4.3 Reports of first trimester miscarriage have been received for both vaccines, both with and without other reactions to the vaccine being reported for the same cases. Based on the number of reports received, the rate of miscarriages for the Oxford-AZ vaccine (23%) is similar to the 25% background rate expected in the UK, whereas the reporting rate for the Pfizer-BioNTech vaccine is currently higher (54%). The EWG noted that data on numbers of vaccinations administered to pregnant women are not yet available to give an accurate estimate of miscarriage rates and that data from the USA for this and the Moderna vaccine has shown a lower miscarriage rate than expected from background.

4.4 A few reports of preterm deliveries following third trimester vaccination have been received but pregnancy outcomes for the majority of 2nd and third trimester vaccines are not yet known.

4.5 The EWG noted that pregnancy carries an elevated risk of blood clots due to hypercoagulability especially in later pregnancy and postpartum. One case of deep vein thrombosis in a leg had been reported following a third trimester vaccination which was being treated according to standard obstetric practice.

4.6 Overall, the EWG considered that the current data are limited but do not raise any particular safety concerns.

4.7 The EWG noted that randomised controlled trials in pregnant women are proposed for the Pfizer-BioNTech vaccine and for the Janssen vaccine (not yet authorised in the UK) whilst an observational cohort study is proposed to investigate safety of the Oxford-AZ vaccine in pregnancy.

5. Discussion on update of thromboembolic events associated with thrombocytopenia reported following COVID-19 vaccination

5.1 The EWG was presented with an update on the issue of thromboembolic events with thrombocytopenia; a review of cases of thromboembolic events associated with thrombocytopenia following vaccination with COVID-19 Vaccine AstraZeneca; a review of cases of thromboembolic events associated with thrombocytopenia following vaccination with other COVID-19 vaccines and a presentation of epidemiological data.

5.2 The EWG heard an updated summary of actions regarding the issue of thromboembolic events and thrombocytopenia, which included:

- temporary suspension of use in people aged less than 55 years in Canada by the Public Health Authority,
- a recommendation by the German Standing Committee on Vaccination (STIKO)

- MHRA's statement on 18th March which communicated the Expert Working Group (EWG) advice that the available evidence currently does not suggest blood clots in veins (venous thromboembolism) are caused by COVID-19 Vaccine AstraZeneca, and that a further, detailed review into a very rare and specific type of blood clot in the cerebral veins (sinus venous thrombosis) occurring together with lowered platelets (thrombocytopenia) is ongoing.
- EMA made a similar statement on 18th March with a decision to update the product information while further investigations were ongoing.

5.3 The EWG was presented with some background information and background rates of thromboembolic events, cerebral venous sinus thrombosis (CVST) specifically, and thrombocytopenia. It was noted that both thrombosis and thrombocytopenia are known to occur in COVID-19 infection - occasionally with mild disease and even after recovery from acute infection. There is also a correlation of these events with severe disease and death.

5.4 The EWG heard that cases reported to MHRA have been evaluated and validated using the WHO-UMC causality assessment system and the case definition which had been established by the EWG and invited haematology experts. The case definition is as follows:

- Confirmed case: Venous/ arterial thrombosis + Platelet count < 150 + D-dimer > 4000 + anti-PF4 antibodies
- Probable: Venous/ arterial thrombosis + Platelet count < 150 + D-dimer > 4000
- Possible case: Venous/ arterial thrombosis + Platelet count < 150
- Unlikely: Criteria met for any of the above BUT alternative diagnosis more likely to explain event.
- Criteria not met: only one or none of the criteria met

A summary of the outcomes of case validation and adjudication was presented, with case details and the validation results provided as an annex in advance of the meeting. Summary details of reported sex and a breakdown of reported ages per classification category were also presented.

5.5 The EWG noted the invited haematology expert's considerations from the adjudication of cases and the difficulties in evaluating the data due to insufficient information in some reports such as the sequence of events (and therefore ability to discern whether cases were predominantly thrombotic or haemorrhagic). The EWG noted the expert's comment that some cases were atypical in that they reported CVST with haemorrhages (which was uncommon), and also that haemorrhage would be unusual if the events are due to a HITT-like mechanism. However, neurologists felt that haemorrhage does occur in patients with CVST even in the absence of thrombocytopenia.

5.6 The EWG discussed the case definition and concluded that it was appropriate and is currently broad enough to capture possible cases and that it can be narrowed and refined as we learn more. The EWG commented that both venous and arterial thromboembolic events should be included in the case definition and that there was not a need to specify a time to onset until a proposed mechanism is better understood.

5.7 The EWG commented that a better understanding of the rate of PF4 antibody positivity in the vaccinated population in general and in people who had had a COVID-19 infection would be valuable. Public Health England informed the EWG of plans underway to gather data on background presence of antibodies to PF4 using samples from older vaccine recipients, unvaccinated individuals and convalescent samples.

5.8 The EWG noted recent literature which quoted the background rate of CVST as 15 per million per year, with 5% mortality. The number of cases and those that were fatal were therefore of significance. The EWG considered that there may be more reporting of such events in younger age groups as they may be less recognised, diagnosed and investigated in older people. In the elderly, symptoms may be ascribed to an ischaemic stroke without undertaking a CT venogram potentially underestimating the incidence of CVST in the elderly. The EWG also considered that differences in the deployment strategies between the AstraZeneca and Pfizer vaccines may affect reporting of potential cases, as elderly people in care homes mostly received the Pfizer vaccine.

5.9 The EWG heard that work was ongoing with collaboration between neurologists and haematologists to establish background rates using neurology and radiology centre data on CVST events and linking it to records of the patients' platelet counts.

5.10 The EWG discussed possible mechanisms for the events reported. A HITT-like mechanism has been proposed by international research groups, due to the presence of anti-PF4 antibodies in some affected patients. It was noted that PF4 can be stimulated by inflammatory responses and that there were likely many conditions that can stimulate PF4, with tuberculosis being one example. The EWG commented that it could be associated with the PF4 antibodies plus a currently unknown other factor(s). Nevertheless, the EWG noted that it could take a long time to identify a mechanism.

5.11 The EWG considered that the onset times of the reports showed a temporal association with vaccination. However, they noted that the pattern seen in onset times could be due to a healthy vaccinee effect following vaccination and then fewer cases with longer onset times due to a lack of longer follow-up time after vaccination and a detection bias in cases with longer onset times.

5.12 The EWG concluded that while there was a temporal association between vaccination and the reported events, the mechanism had not been confirmed and thus a causal association with the AstraZeneca vaccine could not be established. The EWG considered that useful information could be gleaned from data from 2nd doses; however, there currently was not sufficient 2nd dose data to analyse any potential risks.

5.13 The EWG heard that no UK cases of thromboembolic events with thrombocytopenia had been reported for the Pfizer vaccine. However, one case had been reported in Italy (of cerebral venous thrombosis with thrombocytopenia), as well as a Slovenian report of M2 branch thrombus with a low platelet count and an Italian case of pulmonary embolism with thrombocytopenia. Non-UK cases were also validated with the criteria described above. MHRA highlighted a US publication of a series of cases reporting thrombocytopenia within 2 weeks of vaccine with mRNA COVID-19 vaccines. Two cases reported thrombotic events with thrombocytopenia following Pfizer vaccine. MHRA also reported on 1 case from clinical trials and another from post-marketing use of the Janssen vaccine in the US.

5.14 The EWG was presented with statistics on the cumulative exposure to the AstraZeneca and Pfizer vaccines, broken down by age, followed by estimates of the incidence rates of CVST with thrombocytopenia and as well as for all thromboembolic events with thrombocytopenia, broken down by age and gender.

6. An updated epidemiological analysis of the risks of thromboembolic events and potential further study

6.1 The EWG heard the MHRA review of an analysis from PHE of the events of interest associated with the AZ and Pfizer vaccine from hospital admissions data in the UK. The presentation highlighted that there was no indication of a raised risk of thromboembolic

events with either of the vaccines. There was no increased risk identified with the exception of 'Intracranial and intraspinal phlebitis and thrombophlebitis' for which there was indication of a small increased risk for AZ in the under 65 years age group; it was noted that unadjusted confounding could be present and that the numbers were small. The EWG was also informed about an analysis of the benefit of COVID-19 vaccination based on a PHE review. The number of cases of hospitalisation, death and long-COVID prevented per 1 million vaccinations per age group was presented, along with the number of cases and fatal cases of thromboembolic events expected to be reported per 1 million doses.

6.2 The EWG were also presented with opportunities for further epidemiological analysis.

6.3 When discussing the benefit risk in different age groups, the EWG again commented that there could be under reporting of events in elderly people due to a less thorough investigation of neurological symptoms. That being said, the EWG noted that the age distribution seen is typical for CVST events in the non-vaccinated population.

6.4 The EWG discussed whether risk mitigation was needed due to the presence of an alternative vaccine where these events are not seen at the same level, however it was agreed that risk benefit evaluations should be made without consideration of other vaccines.

6.5 The EWG considered that the overall risk of thrombosis with thrombocytopenia remains low but there is concern of significant harm for individual patients. In younger age groups, the risk of COVID-19 and associated complications might not be as high and so the benefit risk from the vaccine in these groups may be different to older groups. It was however noted that while Long COVID is still not well understood, this is an important risk in young people and a potential decrease in this risk would be an additional benefit of vaccination.

6.6 The EWG was not able to identify any specific risk factors but did note that cases with confounding factors should be further investigated to determine if there are any specific populations at risk.

6.7 The EWG concluded that based on current data it not possible to establish an age group where the benefit risk was negative but recognised that irrespective of causality, early identification of such events and correct treatment were needed.

6.8 The EWG commented that the gender bias usually seen with CVST has not been established in the reported cases, which could also suggest a causal link. It was agreed that simple and clear messaging on warning signs is needed so that cases could be identified early, reported in detail and managed clinically.

6.9 The EWG was presented with an overview of planned and ongoing pregnancy studies for the Pfizer and AstraZeneca vaccine, as well as initiated paediatric studies.

6.10 The EWG heard that there was clear support from the Paediatric Medicines Expert Advisory Group for vaccine studies in children with careful evaluation of safety in this population. The EWG considered it reasonable to suggest that children will be at lower risk of these events as thromboembolic risk factors are much lower in children and also there were no documented cases of HITT in children.

6.11 The EWG concluded that paediatric and pregnancy trials should not be stopped at this point, but there needs to further evaluation of the pregnancy trials, and pregnancy exposure to date.

6.12 The EWG advised that the benefit/risk is still overwhelmingly positive, however younger age groups may have risk minimisation needs. Further work is needed on case definition and

case ascertainment will be important. Understanding the background rate of these thromboembolic events with concurrent low platelets will be critical as it is not currently clear if or how much higher above background rates these events are currently occurring. Better mechanistic data is needed to establish causality. Currently a temporal association is seen with vaccination, but causality has not been established.

6.13 The EWG considered it important to communicate what is currently understood about these events with clear, simple messaging in order that vaccine recipients can be appropriately informed. The EWG highlighted the two important audiences for communications; the general population and the healthcare professionals in order to minimise misinformation and establish MHRA evidence as the single point of truth.

6.14 The EWG supported the co-ordination with the EMA and WHO, and to consider lessons learnt from previous high-profile vaccine communications.

6.15 Regarding the content of communications, the EWG advised that the benefits of vaccination should be emphasised in order to contextualise this small potential risk. Information about the potential risk should be provided in absolute terms, with the uncertainties stated. The upper estimate of the risk should be presented, compared to the potential risks from COVID-19 infection.

6.16 The EWG advised that communications should avoid segmenting young vs old or by gender as there are currently too many uncertainties. It should be made clear that it remains a dynamic situation which is still under extensive investigation and advice might change as evidence emerging.

7. Any Other Business

7.1 None.

8. Date and time of next meeting

The next meeting is scheduled to take place on Tuesday 6th April 2021 at 12:30.

The Meeting today started at 11:32 and ended at 14:42.

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.

Annex II

The following participants declared interests and other relevant interests at the meeting today:

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 on 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.

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 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 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 Robertson - Other relevant interest arising from presenting a vaccine safety study alongside Professor Sheikh of Primary Care Research and Development to the EWG on behalf of the EAVE II and DaC-VaP Collaborators.

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.

Mrs Wang - Other relevant interests arising from being highly sensitive to insect stings, and plant products such as Hyacinth bulbs, as recorded on Mrs Wang's medical records. The family of Mrs Wang lives with several rare diseases and conditions, some of which result in epileptic fits.

Professor Weir - NPNS - Imperial College and Other relevant interest arising from his department collaborates with Imperial College on a number of clinical trials.

Observers

Dr [redacted] **-** [redacted]

Professor Wei Shen Lim - NPNS arises from the institution (Nottingham University Hospitals NHS Trust) where Professor Lim works has received unrestricted investigator-initiated research funding from Pfizer for an unrelated prospective population-based cohort study of pneumococcal pneumonia in which Professor Lim is the Chief Investigator.