

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

Minutes of the meeting held on Friday 10th December 2021 at 12:30 via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer
Professor G Dougan
Mr VI G Fenton-May
Professor N French¹
Professor D Goldblatt
Ms S Hunneyball
Professor K Hyrich
Sir M Jacobs
Professor H J Lachmann
Professor P J Lehner
Mr R Lowe²
Dr S Misbah
Professor S Price
Dr A Riordan
Professor K M G Taylor
Dr R Thorpe
Professor M Turner³
Professor S Walsh¹
Mrs M Wang
Professor C Weir

Apologies

Professor Y Perrie
Professor C Robertson
Professor T Solomon

Visiting / Invited Experts

[REDACTED]⁴
[REDACTED]⁵
[REDACTED]⁶
[REDACTED]⁷

Observers⁸

[REDACTED]
[REDACTED]
[REDACTED]

Secretariats

[REDACTED]
[REDACTED]
[REDACTED]

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea – LD
[REDACTED] – VRMM

Presenters supporting specific items⁴

[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] - LD
[REDACTED] - VRMM
[REDACTED] - VRMM
[REDACTED] - LD

MHRA Observers

[REDACTED] - VRMM
[REDACTED] - LD
[REDACTED] - VRMM
[REDACTED] - MHRA-Policy
[REDACTED] - VRMM
[REDACTED] - Comms
[REDACTED] - LD
Dr N Rose - MHRA-NIBSC
[REDACTED] - VRMM
[REDACTED] - MHRA-Policy
[REDACTED] - VRMM
Mr P Tregunno – VRMM

[REDACTED]

23rd June 2022

Key

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

- ¹ left after item 5
- ² left during item 9
- ³ joined during item 4
- ⁴ supported specific items
- ⁵ joined for item 9 only
- ⁶ joined for items 6-8
- ⁷ joined for items 6-9
- ⁸ left before item 9

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 Professors Perrie, Robertson and Solomon for this meeting.

1.5 The Chair welcomed the following visiting / invited experts:

[REDACTED]
[REDACTED] UKHSA

[REDACTED]
[REDACTED] University
of Cambridge

[REDACTED]
[REDACTED] Bristol Heart Institute

[REDACTED]
[REDACTED] University of Edinburgh

1.6 The Chair welcomed the following observers:

[REDACTED]
[REDACTED] Public Health Agency

[REDACTED]
UKHSA

[REDACTED]
[REDACTED]
NHS England and NHS Improvement (National)

2. US Study D8110C00001 Data and resulting AstraZeneca vaccine PI updates

- 2.1** The EWG heard the efficacy results of the US Study D8110C00001. This was a larger dataset than that which was submitted for the initial approval. In addition, the study was designed so that at least 25% of participants were ≥ 65 years of age and participants were to have a 4-week interval between doses.
- 2.2** The positive results seen in the previous submission were confirmed; vaccine efficacy (95% CI) was 73.98% (65.34 – 80.47) well above the standards for vaccine efficacy defined by the WHO (vaccine efficacy of 50% with the lower bound of the 95% CI above 30%).
- 2.3** The EWG heard that the larger dataset allowed provision of reassuring data in a number of areas where there were previously too few cases for independent demonstration of efficacy. Vaccine efficacy by WHO standards was shown independently for the subgroup of participants aged ≥ 65 years, black participants, and against severe or critical symptomatic illness. Consequently, the updated analysis addresses gaps in the data that were highlighted in 2020 during the initial assessment of the meta-analysis.
- 2.4** The EWG heard that previously there had been a concern that dose interval as short as 4 weeks may lead to unsatisfactory efficacy. This concern is allayed by the US study that shows VE to WHO standards with a 4 week dose interval.
- 2.5** On safety, the EWG heard that solicited adverse events were in line with known and expected safety profile. AEs were mild or moderate and short-lived. Unsolicited events - no difference between treatment arms concerning serious AEs within 28 days, medically attended adverse events (MAAEs), adverse events of special interest (AESIs), or number of fatal reports. The EWG heard in line with known safety profile preferred term (PT) unsolicited reports were $>1\%$.
- 2.6** The EWG heard there was a small imbalance in the number of unsolicited related events PTs reported with a frequency $<1\%$. The EWG heard that, except for muscle spasm, the other PTs will not be included in the SPC for reasons specific to the reported events to which they relate
- 2.7** An imbalance between treatment and placebo arm was also observed related to the adverse event of special interest 'facial paralyses and the EU PI will be updated to reflect these new findings. At a EWG meeting April 2021, facial paralysis/ Bell's palsy was reviewed but as no signal was established, close monitoring was recommended. To reflect the updated analysis and to align with the EU position, the assessors proposed to add facial paralysis as an ADR to the SmPC with a frequency 'rare'. The EWG noted this change will need to also be implemented in both the CMA and the temporary authorisation under Regulation 174.
- 2.8** The EWG heard the data analysis relates to end 2020 to beginning 2021. In the clinical assessment report, 88 out of 203 breakthrough cases have had interpretable lineage data available and the predominant variant was B.1.2 a variant defined by Q677P mutation. The EWG noted that this shows the variant was closely related to the wild-type and is a variant that does not appear to impact vaccine efficacy.
- 2.9** The EWG agreed that the data from the US study were reassuring and supported the alignment of GB PI.

3. AstraZeneca booster study and resulting PI updates

- 3.1** The EWG was reminded that the AstraZeneca vaccine was authorised by the national route in Great Britain, however, the aim, where appropriate, is to avoid divergence from the EU product information.
- 3.2** Booster (third dose) data has been submitted to the MHRA by way of variation application to the CMA, but this data has already been reviewed during the Reg 174 procedure on boosters.
- 3.3** The sole clinical data submitted on third dose AZ was taken from a sub-study of COV-001 in healthy subjects (Flaxman et al; 2021, Lancet). After a third dose of vaccine administered 28 – 38 weeks after the second dose, GMT of IgG against Victoria strain increased by almost 2-fold compared to second dose (1926 to 3495) (n=73), neutralising antibodies increased by 2 to 3-fold against alpha, beta, delta variants, and spike (S)-specific T-cell response was boosted at the same level as after the second dose. The EWG heard that, compared to first dose, local reactions were similar, but a much lower frequency and severity of systemic reactions was reported, in line with the reactogenicity of the second dose.
- 3.4** The EWG heard the proposed indication of third (homologous booster) dose at least 6 months after second dose is supported. The assessors also suggest harmonizing with the EU SmPC of other vaccines to include a statement in section 4.2 related to decisions on third doses being based on available vaccine effectiveness data and taking into account the limited safety data.
- 3.5** The EWG discussed Omicron in relation to third doses and concluded that there is no data available on Omicron from AstraZeneca; however, early data on Pfizer indicate that 2 doses afford some protection against Omicron, while a third dose increases protection further but the greatest protection appears to occur in individuals with exposure to previous COVID-19 and vaccine.
- 3.6** The EWG noted that the AstraZeneca booster (third dose) is only being deployed to individuals where there is a medical reason to do so, for example, if an individual requests the AstraZeneca vaccine after a bad experience with another COVID-19 vaccine at second dose. They heard that the number of third doses with AstraZeneca vaccine is small. One area where use of AstraZeneca may facilitate delivery is to housebound individuals, due to the longer shelf life and less constrained storage conditions.
- 3.7** The EWG endorsed the assessment and supported the proposals to update the SmPC of the CMA. It was reminded that this update does not apply to the Reg 174 product information.

4. AstraZeneca study protocols D8111R00010 and D8111R00011

- 4.1** The EWG was presented with two study protocols submitted by AstraZeneca as part of the Risk Management Plan commitment to further assess thrombotic thrombocytopenia syndrome (TTS).
- 4.2** The EWG heard that the first protocol D8111R00010 proposed two observational studies, including a self-controlled case series to estimate the risk of TTS in a given exposure window; and a matched case control study to characterise possible risk factors.
- 4.3** Protocol D8111R00011 is a proposed retrospective cohort study to estimate the incidence of TTS, thromboembolism (TE) and thrombocytopenia (TCP) in general and within a pre-defined time interval of receiving COVID-19 vaccine; and to evaluate possible associations between

TTS and pre-defined risk factors. For this study, three time periods including ‘prior pandemic’, ‘pandemic prior vaccine roll-out’ and ‘pandemic post vaccine roll-out’ will be considered.

- 4.4** The EWG noted that both studies are proposed to use linked healthcare databases in England.
- 4.5** The EWG discussed both protocols and agreed that the case definition for TTS might be a significant limitation. It was suggested that MHRA should receive feedback on TTS case definition in an iterative process once the quality of the databases is clearer rather than waiting for the study report.
- 4.6** The EWG was in agreement that the study conducted as proposed may not obtain much new information compared to other work undertaken in these databases, such as the work by Hippisley-Cox or Andrews and Stowe. The EWG recommended that the inclusion of other EU databases where there was a significant use of AstraZeneca COVID-19 vaccine, such as Scandinavian databases, should be considered and combined with the data from NHS TRE.
- 4.7** With regards to the retrospective cohort study, the EWG raised concern around the adequacy of the follow-up time regarding the control group as the vaccine roll-out was rapid.
- 4.8** In addition to the above recommendations, the EWG supported that the company should be requested to address the proposed MHRA questions raised in sections 4 and 6 of the respective protocol assessment reports.

5. General safety review of COVID-19 vaccine boosters

- 5.1** The EWG was presented with a review of the available safety data on the use of the AstraZeneca, Pfizer/BioNTech and Moderna COVID-19 vaccine booster/third doses. The EWG considered clinical trial data, UK Yellow Card reports (with a data lock point of 1 December 2021), Yellow Card Vaccine Monitor data, data from the companies, published literature and international data.
- 5.2** The EWG noted that the reports received after booster/third doses to date were in line with those seen following primary vaccination and that no new signals were raised in these data. The experts discussed their experience regarding COVID-19 vaccine booster/third doses in clinical practice and commented that they had not encountered any particular concerns with any of the vaccines including with the use of heterologous dosing.
- 5.3** The EWG noted the 20 global reports in association with Moderna COVID-19 vaccine that were grouped in the company’s summary monthly safety review under the term ‘Vaccine-associated enhanced disease (VAED)’. It was confirmed that these were reports of COVID-19 or lack of efficacy in individuals who had received a third dose of Moderna COVID-19 vaccine rather than reports of true VAED.
- 5.4** The EWG noted the use of COVID-19 vaccine Janssen as a booster dose in the United States. The EWG discussed that the World Health Organisation had recently recommended that a second dose of COVID-19 vaccine Janssen may be appropriate in some circumstances. The EWG also discussed that trials in South Africa appeared to show good efficacy of COVID-19 vaccine Janssen against beta and delta variants of COVID-19.
- 5.5** The EWG agreed that no new safety concerns had been identified in either the safety data on the use of the three individual COVID-19 vaccine booster/third doses or in relation to reports recording both COVID-19 vaccine and influenza vaccination. The EWG agreed that the safety data on the use of the AstraZeneca, Pfizer/BioNTech and Moderna COVID-19 vaccine

booster/third doses were reassuring. The EWG highlighted the importance of communicating further reassuring messages regarding COVID-19 booster/third doses following this review.

6. UKHSA Assessment of cardiorespiratory deaths in 15–39-year-olds and COVID-19 vaccination

6.1 The EWG were presented with an analysis from UKHSA of cardiorespiratory deaths in 15–39-year-olds and COVID-19 vaccinations. This analysis was undertaken to investigate whether COVID-19 vaccines may play a role in an observed excess in all-cause mortality in adults in 2021 following the second wave of the pandemic, which could not be explained by COVID-19 deaths alone. The EWG noted that given the observed association between mRNA COVID-19 vaccines and myocarditis the analysis focused on cardiac mortality and sudden death.

6.2 The EWG were informed that death registrations were linked to the NIMS database to obtain vaccine history.

6.3 The EWG noted several factors which may introduce bias into the analysis such as the fact that many deaths in the 15–39-year age group are subject to coroner’s investigations and therefore often take longer to be registered, meaning more recent counts of deaths will be lower than final numbers, along with consideration that data on the clinically extremely vulnerable status of patients may not be complete.

6.4 The EWG were informed that Moderna was not included in the analysis due to low exposure and numbers of outcomes. The EWG noted that there was no signal in the Pfizer data for 15–29-year-olds, and while a marginal increased risk was seen for COVID-19 vaccine AstraZeneca in the 6 days post vaccination, this was based on a small number of events and was likely explained by residual confounding.

6.5 The EWG was informed that no raised incidence was seen for AZ or Pfizer vaccines in the 30–39-year age group, or when the age groups were combined to 15–39-year-olds.

6.6 The EWG also noted some analysis looking at the risk of death following COVID-19 itself, which showed a clustering of events in weeks 4-5 following a positive PCR test.

6.7 The EWG noted that overall, the analysis did not find any convincing evidence of excess cardiorespiratory deaths following either AZ or Pfizer COVID-19 vaccination, and that the reason for the increased all-cause mortality is more likely related to COVID-19 itself as there is an overlap with the third pandemic wave.

6.8 The EWG agreed that in future analyses it would be important to allow time for any delayed registrations of death to be captured, and to consider a wider range of death causes.

7. Protocol review: Low interventional cohort study of myocarditis/pericarditis associated with Comirnaty in persons less than 21 years of age

7.1 The Expert Working Group (EWG) were informed of a company study protocol submitted by Pfizer/BioNTech as part of pharmacovigilance activities outlined in the risk management plan (RMP) regarding the important identified risk of myocarditis and pericarditis with the Pfizer/BioNTech COVID-19 vaccine. This study is a collaboration between National Heart, Lung and Blood Institute (NHLBI) and Paediatric Heart Network) and Pfizer.

- 7.2** The EWG were presented with an overview of the study, which is a post authorisation, low intervention cohort study, located in the US, assessing myo/pericarditis associated with Comirnaty in persons less than 21 years, with the aim to characterise long term risk in this age group (n=200), and comparing these outcomes following myo/pericarditis after COVID-19 infection (n=100) including that associated with Multisystem inflammatory syndrome in children (MIS-C). The EWG heard that the study had a planned follow up over five years and those investigations carried out in study visits would be in line with routine clinical care, and consist of investigations such as cardiac MRI, ECG, echocardiograms and exercise tests.
- 7.3** The EWG heard of potential limitations of the study design, including the potentially unpredictable number of eligible patients, the fact that the risk of myo/pericarditis post vaccination is not well characterised in young age groups, that there may be variation in clinical practice which could impact results, and that the COVID-19 infection comparator group might not be comparable in terms of patient characteristics compared to the vaccinated group.
- 7.4** The EWG heard that the MHRA intended to request the study age group be expanded to 25 years, and this was supported by both invited cardiology experts and EWG members. The MHRA also intended to request the company provide 6 monthly updates on the study, including on recruitment to ensure this is spread evenly across the age group; this was supported by the EWG.
- 7.5** Invited experts highlighted that other causes of myocarditis and pericarditis, outside of Pfizer/BioNTech vaccination and COVID-19 infection, should be excluded. EWG members also commented that the study did not adequately address how relapses of myo/pericarditis would be identified and recorded, and that this was a limitation of the study.
- 7.6** Invited cardiology experts commented that the study was important for contributing to knowledge on the identified risk of myo/pericarditis and long-term outcomes of this. It was highlighted by both invited experts and members that there may be issues with the practicality of repeat investigations, particularly cardiac MRIs, and that adherence to this in the study population might be reduced. General concerns regarding retention of participants throughout the course of the 5 year follow up period were also raised by the EWG, and that this might limit the impact of the results from the study.
- 7.7** The EWG concluded that the study was of value, particularly regarding long term outcomes of myo/pericarditis following COVID-19 vaccination.
- 8. Update of myocarditis and pericarditis following administration of Pfizer/BioNTech, Moderna and AstraZeneca COVID-19 vaccines**
- 8.1** The EWG were presented with an update on the Yellow Card reports for myocarditis and pericarditis with the three COVID-19 vaccines in use in the UK vaccination programme as well as new international data and literature.
- 8.2** The EWG were informed that the reporting rates remained similar between the first and second doses of the Pfizer/BioNTech vaccine and that the reporting rates for both the first and second dose in the under 18 age group had increased slightly but remained lower than the 18-29 age group. The Moderna reporting rates remained similar to the last update, with higher reporting rates after the second dose in the younger age groups and a higher reporting rate when compared to the Pfizer/BioNTech vaccine. For AstraZeneca the reporting rates has remained similar to previous reviews and overall were lower than both of the mRNA vaccines.
- 8.3** The EWG heard that the nature of the Yellow Card reports was similar to that previously presented for the vaccines, with higher proportions of reports in males and in younger age

groups, with reports for the mRNA vaccines seen in younger age groups compared to the AstraZeneca vaccine. The EWG heard that a high proportion of the Pfizer/BioNTech booster reports were with the homologous schedule and that this was different to the general booster reporting for the Pfizer/BioNTech vaccine which had an even split between homologous and heterologous schedules.

8.4 The EWG were presented with international data on fatal reports of myocarditis following COVID-19 vaccination. The EWG discussed the details of the reports and highlighted that there were some inconsistencies with the histopathology in some of the reports, noting that histopathology was a highly specialised area. The EWG considered that the majority of the reports were confounded by concomitant conditions.

8.5 The EWG were presented with a preprint paper with data from a cohort study in Ontario, Canada. The EWG were informed that the study had found that reporting rates of myocarditis and pericarditis were higher after the second dose when there was a shorter interval between the first and second vaccine doses for both Pfizer/BioNTech and Moderna vaccines, with lower reporting rates for longer dose intervals. The EWG considered that the lower rates with the longer dosing interval may explain why the Yellow Card reporting rates show less of a difference between the first and second dose compared to other countries.

8.6 The EWG concluded that the benefits continued to exceed the risks overall for each vaccine and for all authorised subpopulations. No regulatory action was required based on the data presented.

9. Pfizer CMA 5-11-year-old

9.1 The EWG considered a line extension application for Comirnaty (COVID-19 vaccine Pfizer/BioNTech). Comirnaty 30 micrograms/dose concentrate for dispersion for injection is currently indicated for use in individuals aged 12 years. This line extension is to introduce a new paediatric formulation 'Comirnaty 10 micrograms/dose concentrate for dispersion for injection' for use in children 5 to 11 years. The current licensed dose of Comirnaty for the primary immunization course in individuals aged 12 years and over is two doses (30 micrograms / 0.3mL each) administered 3 weeks apart., The subject of the line extension application is a lower dose (10 micrograms / 0.2mL each) of two doses administered 3 weeks apart. The EWG noted that this application has been submitted via the European Commission Decision Reliance Route.

9.2 The EWG heard that a number of regulatory agencies have recently approved Comirnaty 10 micrograms/dose concentrate for dispersion for injection for use in children aged 5 to 11 years including the FDA (29 October 2021), Health Canada (19 November 2021) and the EMA (25 November 2021).

9.3 The EWG heard that data have been submitted from the positive ongoing clinical trial (C4591007) in children aged 5-11 years and the EWG was presented with these data.

9.4 The EWG heard that immunobridging of neutralising antibody levels between children aged 5-11 years and young adults aged 16-25 years has been established. This is supported by a high level of short-term efficacy data in children aged 5-11 years against symptomatic disease after 2 doses of the vaccine, similar to the efficacy seen in adults.

9.5 The EWG heard that the most frequent adverse reactions in 5 - 11 year olds were injection site pain (>80%), fatigue (>50%), headache (>30%), injection site redness and swelling (>20%), myalgia and chills (>10%). When the reactogenicity data in children aged 5-11 years was compared with that in 16-25 year olds in study C4591001, rates of pain at the injection

site were slightly lower in the 5-11 year-old group, but redness and swelling slightly higher. Systemic adverse reactions such as fever, fatigue, headache, chills, and muscle pain were generally reported less frequently and were milder in severity in the 5-11 year-old group. No deaths were reported up to the data cut-off of the study and very few serious adverse events were reported, none of which were considered related to the study vaccine.

- 9.6** The EWG noted that no new safety concerns have been identified from the clinical trial data in children aged 5 to 11 years. The only difference in the table of adverse drug reactions in the summary of product characteristics is a footnote to indicate that ‘Injection site redness’ occurred at a higher frequency (very common vs common) in children aged 5-11 years.
- 9.7** The EWG were also provided with an update on the quality aspects, conditions, and the available post authorisation safety data (GB YC reports from accidental use predominantly in children that were close to the upper bound of the age range, and safety data gathered by other national competent authorities).
- 9.8** The EWG noted that the extension product formulation (10 microgram) differs only in fill volume and the differences in the dilution steps. The EWG also noted that measures taken to distinguish the 10 microgram product from the 30 microgram presentation appear appropriate. The EWG noted the product labelling will need to convey the different dilution process. The EWG supported alignment of in-use storage conditions with the requirements on unpreserved vaccines. The EWG supported the assessment of dossier on quality.
- 9.9** The EWG heard an overview of the Risk Management Plan (RMP).
- 9.10** The EWG considered that the clinical trial data on immunogenicity and efficacy in children aged 5 to 11 years are good and are similar to that seen in older age groups. The EWG also considered that the early safety data are reassuring. The EWG agreed with the clinical assessor’s recommendation that an additional GB specific condition be added to the Conditional Marketing Authorisation whereby the company should submit longer-term 6-month safety follow-up data in children aged 5-11 years from the clinical study C4591007 once available.
- 9.11** The EWG reasoned that an unmet clinical need exists for vaccination in the lower age group (5-11 years) because the number of children affected by COVID-19 is becoming significant, as are the impacts of this virus on this age group.
- 9.12** The EWG also noted that ~250,000 children Canada and Israel aged 5 to 11 years have been vaccinated and no cases of myocarditis have been reported.
- 9.13** The EWG noted that the risk-benefit analysis conducted by the FDA carries limitations but appears to be a reasonable approach to present a more holistic risk-benefit picture of myocarditis risk versus benefits from vaccination in this age group. The benefit risk is preserved in the model with the lowest COVID incidence rate.
- 9.14** The EWG mentioned it would be beneficial to see granularity in the FDA data, for example, data that relate to the rate and case histories of COVID-19 related myocarditis in 5-11 year olds. The EWG also noted that the background cases of myocarditis are lower in 5-11 year olds when compared to rates seen in the 12-15 year olds.
- 9.15** The EWG also discussed the rate cases of seizures in the post marketing reports, thought by the FDA, to be mis-classified reports that may instead relate to myoclonic activity associated with a vasal-vagal episode. The EWG noted vasal-vagal episodes were more likely to occur in older teenagers and, are perhaps less likely to occur in 5-11 year olds. However, it was

thought that the seizures were unlikely related to febrile fits, as the EWG noted these most commonly occur in children aged 5 and under. To help unravel potential cause/s of these cases of seizures, the EWG suggested that further data is requested.

- 9.16** The EWG noted that text in the package leaflet on myocarditis could be tailored to reflect the data in the younger age group/population. The EWG also noted there was an opportunity to provide text in the product information aimed directly to recipients (children) alongside the information directed to parents/guardians.
- 9.17** The EWG noted including the 5-11 year olds in the post-authorisation safety study/ies (PASS) was a positive step and advised that, once data are available, stratification by age will be necessary in the presentation of these data.
- 9.18** The EWG agreed that this EC reliance procedure can be approved.

10. Any Other Business

- 10.1** The EWG were informed that data on GBS and the AstraZeneca vaccine was expected to be published shortly.

11. Date and time of next meeting

The meeting scheduled for Friday 17th December has been **cancelled**.

There is a tentative meeting rescheduled on **Wednesday 22nd December at 2.00pm**. Further information will be sent in due course.

The Meeting today started at 12:34 and ended at 16:02.

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

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.

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. Other relevant interest in AstraZeneca arising from being part of a collaboration in which the epidemiology and therapeutic approaches to Vaccine associated Thrombosis-Thrombocytopenia (VITT).

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). Member of the independent Data Safety Monitoring Board for COV-BOOST trial.

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

■ ■■■■■ – Other relevant interest in Pfizer & GSK. The Immunisation and Countermeasures Division has provided vaccine manufacturers (including Pfizer and GSK) with post-marketing surveillance reports on pneumococcal and meningococcal infection which the companies are required to submit to the UK Licensing authority in compliance with their Risk Management Strategy. A cost recovery charge is made for these reports.