

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

Minutes of the meeting held on **Tuesday 29<sup>th</sup> March 2022** at **10:30** via videoconference

**Participants Present**

**Members**

Professor Sir M Pirmohamed (Chair)  
Professor J Breuer  
Mr VI G Fenton-May  
Professor N French  
Professor D Goldblatt  
Ms S Hunneyball  
Professor K Hyrich  
Dr S Misbah  
Dr A Riordan  
Professor C Robertson<sup>1</sup>  
Professor K M G Taylor  
Dr R Thorpe  
Professor S Walsh  
Mrs M Wang  
Professor C Weir

**Apologies**

Professor G Dougan  
Sir M Jacobs  
Professor H J Lachmann  
Professor P J Lehner  
Mr R Lowe  
Professor Y Perrie  
Professor S Price  
Professor T Solomon  
Professor M Turner

**Invited Expert**

██████████<sup>2</sup>

**Observers**<sup>3</sup>

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**Secretariat**

██████████  
██████████

<sup>1</sup> left during item 7

<sup>3</sup> observed for items 3 to 6

<sup>2</sup> participated for item 3 & 4 <sup>4</sup> supported specific items

**Professional Staff of MHRA Present**

**Principal Assessors**

Dr J Bonnerjea - LD  
██████████ - VRMM<sup>4</sup>

**Presenters supporting specific items**<sup>4</sup>

██████████ - LD  
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██████████ - VRMM  
██████████ - LD  
██████████ - VRMM  
Dr S Hopper - LD  
Dr N Rose - MHRA-NIBSC

**MHRA Observers**

██████████ - VRMM  
██████████ - LD  
Dr S Branch - VRMM  
██████████ - LD  
██████████ - LD  
██████████ - VRMM  
██████████ - MHRA-Policy  
██████████ - VRMM  
██████████ - VRMM  
██████████ - VRMM  
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██████████ - LD  
██████████ - Comms

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23<sup>rd</sup> June 2022

**Key**

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

**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 Mr Lowe, Professors Dougan, Lachmann, Lehner, Perrie, Price, Solomon, Turner and Sir Michael Jacobs for this meeting.

**1.5** The Chair welcomed the following invited expert who joined for item 4 - PHS safety surveillance analyses – Acute renal failure:

[Redacted]  
[Redacted]  
[Redacted] Public Health Scotland

**1.6** The Chair welcomed the following observers to the meeting:

[Redacted]  
[Redacted]  
[Redacted] UKHSA

[Redacted]  
[Redacted] Public Health Scotland

[Redacted]  
NHS England [Redacted]  
[Redacted]  
[Redacted]

[Redacted]  
UKHSA

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

**2. Valneva Vaccine**

2.1 A Conditional Marketing Authorisation was recommended for Valneva vaccine. [REDACTED]

2.2 [REDACTED]

**3. Public Health Scotland safety surveillance analyses – Acute renal failure**

3.1 The EWG were presented with safety surveillance analysis from Public Health Scotland relating to acute renal failure. Hospital admissions data were reviewed using ecological population-based interrupted time-series analysis, observed vs expected analysis and a self-controlled case series. The analysis covered individuals aged 12 years and over who received either the AstraZeneca or Pfizer/BioNTech vaccine up to 8 September 2021.

3.2 The EWG were informed that the interrupted time-series analysis showed an upward trend in acute renal failure admissions in the pre-pandemic (2015-2019) period, followed by a lower rate of admissions in the pandemic period. There was an increase in admissions in the vaccination period (first quarter of 2021). Admissions in the vaccination period were lower than the pre-pandemic period but higher than the pandemic period.

3.3 The EWG were informed that the observed vs expected analysis did not show an increased risk of renal failure in the overall and Pfizer/BioNTech vaccine analysis; however, there was an increased risk ratio for the AstraZeneca vaccine compared with the pandemic period.

3.4 The EWG were informed that the self-controlled case series did not show a statistically significant increase in risk for either the overall or AstraZeneca vaccine analysis. For the Pfizer/BioNTech vaccine analysis, a statistically significant increase was seen for the second dose in the 7-, 21- and 42-day risk windows.

3.5 Public Health Scotland concluded that there was some evidence of an increase in renal failure admissions during the vaccination period compared to the pandemic period but not compared to the pre-pandemic period. The EWG considered this may be explained by the overall reduced number of hospital admissions during the pandemic period.

**4. Renal failure and renal impairment following administration of Pfizer/BioNTech, Moderna and AstraZeneca COVID-19 vaccines**

**4.1** The EWG were presented with a review of the Yellow Card reports of renal failure and impairment, observed vs expected analysis and relevant literature.

**4.2** The EWG were presented with the UK Yellow Card reports for the Pfizer/BioNTech, AstraZeneca and Moderna COVID-19 vaccines. The EWG noted that the reporting rate of renal failure events was low for all three vaccines. The majority of events occurred in older individuals with an onset time of approximately 20 days after vaccination. The EWG considered that the majority of reports had significant comorbidities. The EWG noted that the three reports for the Pfizer/BioNTech vaccine in adolescents included other plausible causes for the renal failure events.

**4.3** The EWG were presented with the observed vs expected analysis, which did not identify a signal for increased risk of acute kidney injury within the 7- or 42-day risk window for any of the vaccines. The observed vs expected analysis also found no signal for any age groups for narrow or broad definitions of renal failure.

**4.4** The EWG were presented with a review of the available literature on renal failure and COVID-19 vaccines. The EWG noted that the literature articles related to individual case reports and covered a variety of renal conditions.

**4.5** The EWG considered the totality of the available data from the Yellow Card reports, published literature and analysis by Public Health Scotland. The EWG concluded that as many of the reports contained significant comorbidities that confound the reports, no association to the COVID 19 vaccines could be established. The EWG noted the comprehensive approach to the Public Health Scotland analysis, with multiple study designs used, but noted the challenges with comparing hospital admissions with the pandemic period where non-COVID admissions were lower. The EWG concluded that no regulatory action was required and that reports of renal failure should continue to be monitored.

**5. COVID-19 vaccine safety review in 5-11 years**

**5.1** The EWG was presented with a review of the available safety data regarding the use of the Pfizer/BioNTech COVID-19 vaccine in 5- to 11-year-olds. The EWG considered clinical trial data, UK Yellow Card reports (with a data lock point of 23 March 2022), Yellow Card Vaccine Monitor data, data from the companies, published literature and extensive international experience in this age group.

**5.2** The EWG were also presented with an update on the MHRA's Vaccines Safety Surveillance Strategy in children and adolescents and a proposal to focus the strategy on Adverse Events of Special Interest for this age group, given the current reassuring data following extensive use of COVID-19 vaccines in children aged 5-11 years internationally.

**5.3** The EWG noted that the totality of the data provided reassurance on the safety of the Pfizer/BioNTech vaccine in 5- to 11-year-olds and that no new safety concerns were raised in the data. The EWG noted the small number of Yellow Card reports of seizure in this age group, predominantly in patients with a medical history of epilepsy. It was agreed that seizure cases in 5- to 11-year-olds would be monitored closely moving forward as part of the Adverse Events of Special Interest. It was noted by the EWG that in the international

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data there were lower reporting rates for myo/pericarditis in the 5-11 year age group compared to adolescents and young adults.

**5.4** The EWG noted the data regarding the low reporting rates of anaphylaxis and agreed with MHRA's proposal that the suspension of the 15-minute observation period for the Pfizer/BioNTech vaccine in 5- to 11-year-olds remains in place and closely monitored.

**5.5** The EWG endorsed the proposed refinements to the MHRA's Vaccines Safety Surveillance Strategy for children and adolescents and no further regulatory action regarding the use of Pfizer/BioNTech vaccine in 5- to 11-year-olds was proposed at this stage.

**6. Capillary Leak Syndrome and COVID-19 mRNA vaccines**

**6.1** The EWG were presented with an updated assessment of the data on capillary leak syndrome (CLS) with the Moderna and Pfizer/BioNTech COVID-19 vaccines. It was noted that regulatory action had previously been taken to include CLS as an adverse event for the AstraZeneca and Janssen vaccines as well as including a contraindication in patients with prior history of CLS.

**6.2** The EWG were presented Yellow Card and company data on CLS for the Moderna and Pfizer/BioNTech vaccines. The EWG noted that the reports of CLS did not suggest an association between the mRNA vaccines and new onset of CLS. The EWG were informed that there was differing levels of evidence for flare-up of CLS for Moderna and Pfizer/BioNTech, with 3 Moderna reports meeting the World Health Organisation (WHO) probable criteria while only 1 Pfizer/BioNTech report met the WHO possible criteria. The EWG noted while this was a very small number of reports compared to the total doses administered, the number of patients with CLS having received a vaccine (estimated at 250 for Moderna and 1000 for Pfizer) were much lower.

**6.3** The EWG were presented a paper on the EurêClark registry, consisting of 30 CLS patients. The paper highlighted the risk of CLS flare-up following COVID-19 infection, with 5 patients, all unvaccinated, experiencing a relapse following infection, with a fatal outcome in 4 patients. The EWG noted the importance of ensuring prophylactic measures against COVID-19 were available to CLS patients and considered that a contraindication in patients with a history of CLS should not be added for the Moderna or Pfizer/BioNTech vaccines.

**6.4** The EWG were informed that European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) had concluded that a warning regarding flare-up of CLS should be added to the Moderna vaccine product information, although no update was required for the Pfizer/BioNTech vaccine. PRAC also concluded that there was no association between the mRNA vaccines and new onset CLS and that no contraindication in patients with a history of CLS was required.

**6.5** The EWG concluded that the available data supported the inclusion of a warning in the Moderna vaccine product information regarding flare-up of CLS, in line with the PRAC conclusion. The EWG supported requesting Pfizer/BioNTech to continue to monitor reports of CLS as part of their bimonthly summary safety reports.

**7 For Information - Spikevax dispersion for injection – variation PLGB 53720/0002 – 0090**

7.1 The EWG heard that the MHRA is recommending the grant of this ECDRP variation to section 4.2 of the SmPC. The variation will recommend that Spikevax may be used to boost adults who have received a primary series comprised of another mRNA vaccine or adenoviral vector vaccine. The variation will also reduce the interval between the primary series and the booster dose from at least 6 months to at least 3 months.

7.2 [REDACTED]

7.3 [REDACTED]

**8. Update on potency assay for Comirnaty & Vaxzevria vaccine**

8.1 [REDACTED]

**9. Any Other Business**

None.

**10. Date and time of next meeting**

The next meeting has been scheduled for **Wednesday 13<sup>th</sup> April 2022 at 10:30.**

The Meeting today started at 10:32 and ended at 12:55.

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**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 3<sup>rd</sup> 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.

**Dr Misbah** - NPNS - Holds honorary Senior Lectureship with University of Oxford & Oxford University Hospitals NHS Foundation Trust.

**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.

**Professor Robertson** - Other relevant interest – Professor Robertson assisted in setting up the study for PHS safety surveillance analyses in acute renal failure.



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**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.

**Invited Expert**

██████████ - Lapsed and NPNS - Regarding companies to declare interests for, prior to joining Public Health Scotland, ██████████ worked for a company that provided epidemiological services to the pharmaceutical industry. Whilst working there, ██████████ supported respiratory vaccine development activities at ██████████ ██████████ ██████████ has now left that role.

**Observer**

██████████ – 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.