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

Minutes of the meeting held on Thursday 25th August 2022 at 11:30 via videoconference

# Participants Present

## **Members**

Professor Sir M Pirmohamed (Chair) Professor J Breuer Professor G Dougan Mr VI G Fenton-May Professor D Goldblatt Ms S Hunneyball Dr S Misbah Professor Y Perrie Dr A Riordan<sup>1</sup> Professor C Robertson Professor K M G Taylor Dr R Thorpe<sup>1</sup> Professor S Walsh<sup>2</sup> Mrs M Wang

## **Apologies**

Professor N French Professor K Hyrich Professor H J Lachmann Professor P J Lehner Mr R Lowe Professor S Price Professor M Turner Professor C Weir

#### **Invited Experts**



## **Observers**



## Professor W S Lim

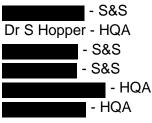




# Professional Staff of MHRA Present Principal Assessors

Dr J Bonnerjea - HQA - S&S

## Presenters supporting specific items



#### MHRA Observers

- S&S - HQA

## **Government Legal Team**



18<sup>th</sup> November 2022

- <sup>1</sup> left during discussions of item 4
- <sup>2</sup> joined during discussions of item 2
- <sup>3</sup> joined to participate in item 2 only
- <sup>4</sup> joined to participate in item 3 only

#### Key

HQA = Healthcare Quality & Access Group S&S = Safety & Surveillance Group **OFFICIAL – SENSITIVE COMMERCIAL** 

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1.6

## 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 French, Hyrich, Lachmann, Lehner, Price, Turner, Weir and Mr Lowe for this meeting.
- **1.5** The Chair welcomed the following invited experts to the meeting:

University of Edinburgh	
Cardiff School of Medicine	
For Item 3: Nuvaxovid and Myocarditis	
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of Cambridge	University
The Chair welcomed the following observers to the meeting:	
UKHSA	

**Public Health Scotland** 

For Item 2: AstraZeneca vaccine and ADEM

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NHS England	
Professor Wei Shen Lim Chair of JCVI	

NHS England and NHS Improvement (National)

# 2. COVID-19 vaccine AstraZeneca and acute disseminated encephalomyelitis (ADEM)

- 2.1 The EWG were presented with a review of the currently available evidence regarding the risk of acute disseminated encephalomyelitis (ADEM) with the COVID-19 vaccine AstraZeneca. The EWG considered data from clinical trials, published literature case reports, spontaneous sources, including Yellow Card data with a data lock point of 27th July 2022, and internal observed versus expected analyses. This paper also considered 6-monthly PSUR reviews undertaken by the company and data identified from other regulatory authorities.
- 2.2 The EWG were informed that there have been 14 spontaneously received UK suspected reports for COVID-19 vaccine AstraZeneca and the narrow search criteria of the preferred term, ADEM. The reporting rate was considered low in the context of both the usage of these vaccines and the background incidence of ADEM, although the EWG did note the diagnostic complexity of ADEM in adult populations that may contribute to under-reporting. Internally conducted observed versus expected analyses did show an increased signal in the 50-59 years age group following the first dose of COVID-19 vaccine AstraZeneca; however the analysis noted the potential for overestimation given the lack of confirmed ADEM cases and lack of precision due to the small number of reports.
- 2.3 The EWG were informed that the company 6-monthly PSURs identified a cumulative total of 54 reports of ADEM. Company observed versus expected analysis showed variability, making meaningful conclusions difficult to draw. The company concluded that the data presented in the PSURs did not establish a causal relationship between COVID-19 vaccine AstraZeneca and ADEM and committed to ongoing monitoring.
- 2.4 The EWG were informed that the European Medicine Agency's Pharmacovigilance Risk Assessment Committee (PRAC) have reviewed the signal of ADEM with COVID-19 vaccine AstraZeneca as presented in the 6-monthly PSURs. The PRAC concluded that the available evidence did not support a causal association, and that this signal should continue to be monitored closely as more relevant information is expected from a Post-Authorisation Safety Study (PASS) using secondary databases.
- 2.5 The EWG and invited neurological experts considered that given the link between COVID-19 vaccine AstraZeneca and other neurological events such as Guillain-Barré syndrome and transverse myelitis, an association could not be excluded based on the limited available data. The EWG offered suggestion of working with UKHSA to investigate the feasibility of a self-controlled case study to characterise this risk further. The EWG noted

that the epidemiology of the condition was not clear cut and the meeting agreed that the totality of the evidence currently available did not indicate a causal association.

**2.6** The EWG endorsed the conclusions that no immediate regulatory action was required, with the understanding that the this would continue to be closely monitored by the MAH and further evaluation with additional data sources undertaken where appropriate.

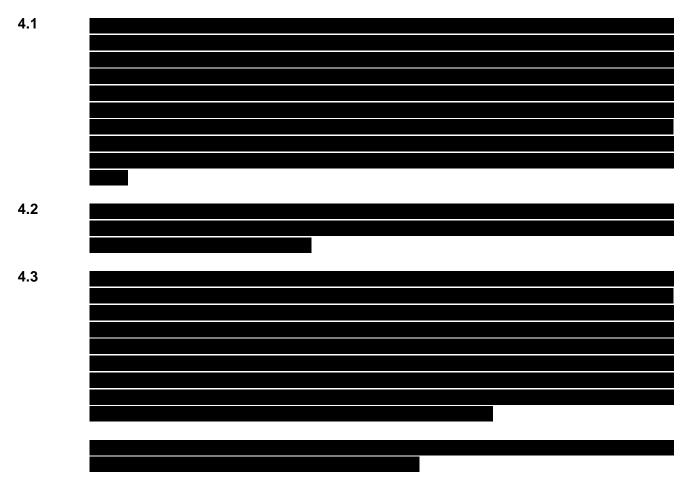
#### 3. Nuvaxovid and myocarditis: EU proposed update to the product information

- **3.1** The EWG considered an updated review of myo/pericarditis in association with Novavax COVID-19 vaccine including the EU Pharmacovigilance Risk Assessment Committee (PRAC) updated assessment of this issue. Data considered in the updated review included clinical trial data, post-marketing reports and company reviews and observed versus expected analyses of myo/pericarditis presented in the fifth Summary Safety Report for Novavax COVID-19 vaccine.
- 3.2 The EWG noted in an updated observed versus expected analysis of myocarditis/pericarditis in the post crossover phase of the clinical trials, when a risk period of 14 days was used in line with the risk window for myo/pericarditis observed with mRNA COVID-19 vaccines, more cases were reported than expected for Novavax COVID-19 vaccine. The EWG also noted that the company had identified 68 post-marketing reports of myo/pericarditis in association with Novavax COVID-19 vaccine using broad search criteria. In total, 26 of these cases were adjudicated by the company to meet possible, probable, or definite Brighton Collaboration case definitions for myocarditis and/or pericarditis, with the remaining reports lacking sufficient information for adjudication.
- **3.3** The EWG noted that, based on the data now available, PRAC had recommended that the EU product information for Novavax COVID-19 vaccine should be updated to include a warning about myocarditis and/or pericarditis and to list myocarditis and pericarditis as undesirable effects with Nuvaxovid. The EWG also noted that a warning about myo/pericarditis was already included in the US product information for Novavax COVID-19 vaccine and that pericarditis was listed as an adverse reaction from post-marketing experience in the product information for Novavax COVID-19 vaccine in Australia and New Zealand.
- **3.4** The EWG considered that there was sufficient evidence to align with the position of other international regulators to include a warning about myo/pericarditis in the GB product information for Novavax COVID-19. The EWG advised that the warning should alert healthcare professionals and vaccine recipients about the possible risk of myo/pericarditis with Novavax COVID-19 vaccine in line with the advice given in the warnings about this risk in the product information for mRNA COVID-19 vaccines.
- **3.5** The EWG heard that, while Novavax COVID-19 vaccine was not currently being deployed in the UK, this vaccine would be used off-label in the Autumn COVID-19 vaccine booster campaign as alternative to mRNA COVID-19 vaccines in people who were intolerant, allergic, or suspected to be allergic to mRNA COVID-19 vaccines. The EWG noted Novavax COVID-19 vaccine would be used in specialist vaccination clinics after individual patient consultations and that, given the likely complex medical history of these patients, they would routinely be observed for 30 minutes after vaccination rather than the 15 minutes wait advised in the Novavax COVID-19 vaccine product information.
- **3.6** The EWG discussed that currently there was no evidence on the risk of myo/pericarditis with a booster dose of Novavax COVID-19 vaccines patients who had previously experienced myocarditis or pericarditis following receipt of an MRA COVID-19 vaccine.

The EWG advised that decision to use Novavax COVID-19 vaccine in such circumstances would need to be based on clinical need and individual risk/benefit assessment.

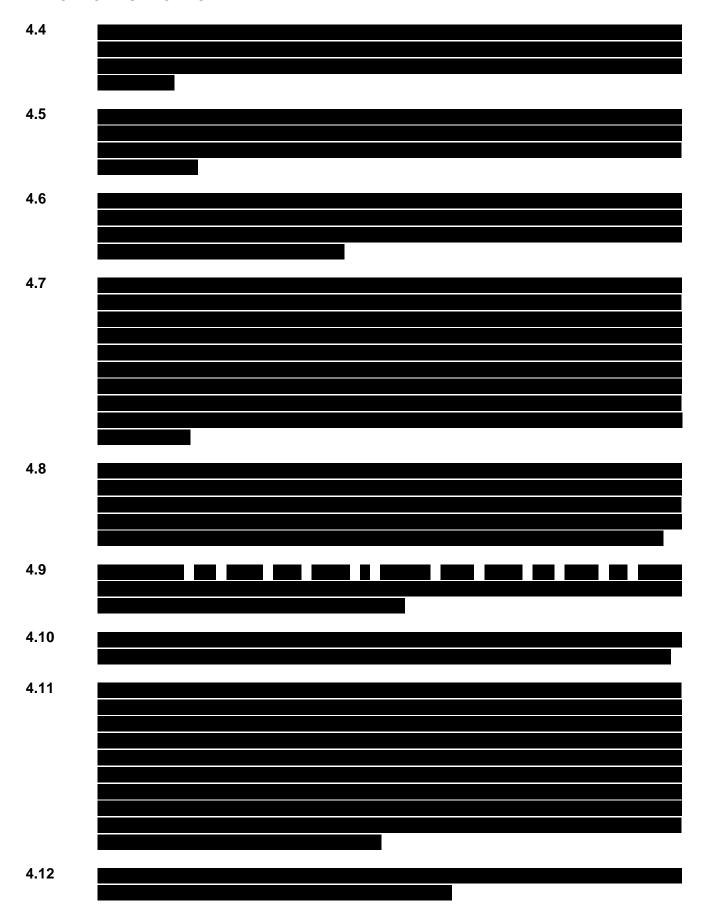
- **3.7** The EWG discussed possible mechanisms for myo/pericarditis after vaccination against COVID-19. The EWG proposed that as myo/pericarditis had now been observed with Novavax COVID-19 vaccine as well as mRNA COVID-19 vaccines, this may suggest that the risk could be related to the spike protein common to the vaccines, rather than a specific risk with the mRNA platform used in the Pfizer and Moderna COVID-19 vaccines. The EWG commented that in the future it would be helpful to review the available data on myo/pericarditis with Pfizer, Moderna, Novavax and AstraZeneca COVID-19 vaccines and COVID-19 itself to see if there was a spectrum of risk for the signal of myo/pericarditis across each of the vaccines.
- **3.8** The EWG requested an update on the work carried by the Marketing Authorisations Holders on possible mechanisms of myo/pericarditis in association with Pfizer and Moderna COVID-19 vaccines. The EWG also advised that Novavax should also be asked what they are doing in relation to looking at potential mechanisms for myo/pericarditis with Novavax COVID-19 vaccine.
- **3.9** Overall, the EWG agreed that the available data supported updating the Novavax COVID-19 vaccine product information in line with the PRAC proposed update to EU product information to include a warning about myocarditis and pericarditis and to list myocarditis and pericarditis. The EWG also agreed that the benefit risk balance of Novavax COVID-19 vaccine remains positive.





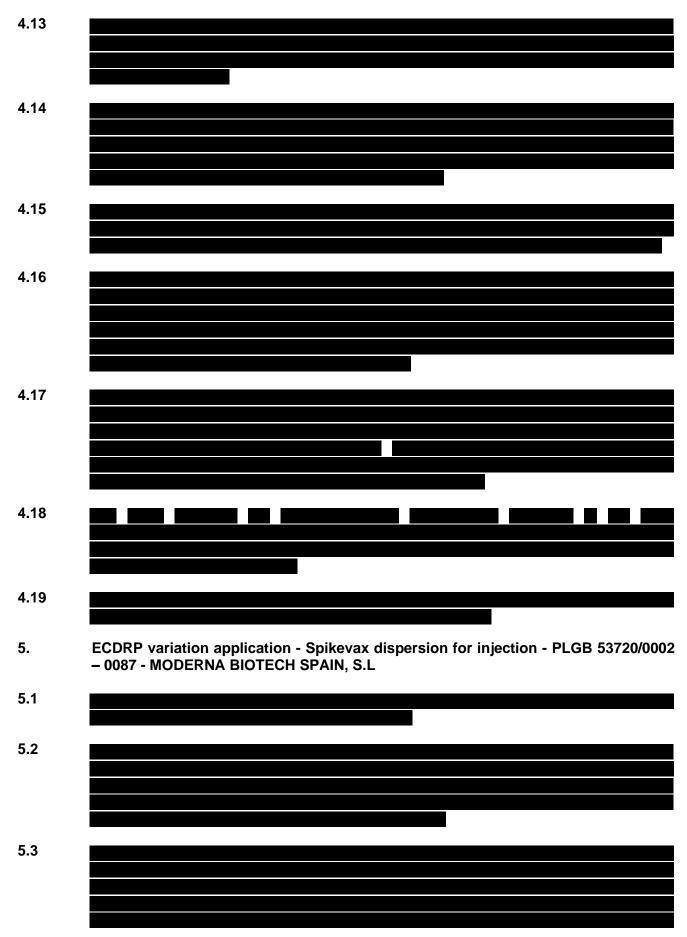
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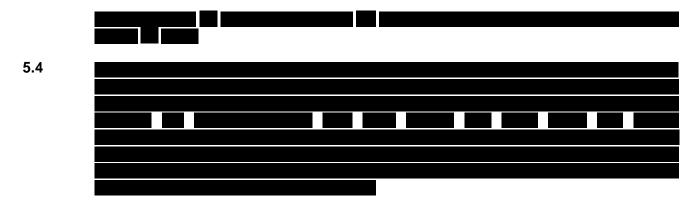
# OFFICIAL – SENSITIVE COMMERCIAL CHM/COVID19VBREWG/2022/16<sup>th</sup> MEETING

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## 6. <u>Minutes of the following meetings for approval</u>

- Monday 5<sup>th</sup> July 2021
- Tuesday 3<sup>rd</sup> August 2021
- Thursday 19<sup>th</sup> August 2021
- Friday 10<sup>th</sup> September 2021
- Thursday 13<sup>th</sup> January 2022
- **6.1** All relevant post meeting queries have been resolved including typo/grammar amendments. Therefore, the above minutes have been endorsed as a true and accurate record of the proceedings.

## 7. <u>Any Other Business</u>

7.1 None.

#### 8. Date and time of next meeting

The next meeting has been scheduled for **Thursday 9<sup>th</sup> September 2022** at **11:30**.

The Meeting today started at 11:30 and ended at 14:00.

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** - <u>NPNS</u> AstraZeneca - Research grant to UOL to support PhD in drug interactions.

<u>Other relevant interests</u> 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-**<u>NPNS</u> – 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).

**Ms Hunneyball** - <u>Other relevant interest</u> – 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.

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

**Professor Perrie** - <u>NPNS</u> 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).

**Dr Riordan** - <u>Other relevant interests</u> - Participant in Oxford University's ChAdOx1 nCoV-19 clinical trial –received immunisation 27/8/2020. <u>NPNS</u> - 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** - <u>Other relevant interests</u> 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.

## <u>Observer</u>

 Other relevant interest – The Immunisation Dept at PHE does sell surveillance reports on Meningococcal and Pneumococcal vaccination and disease on cost recovery basis to GSK and Pfizer.

**Professor Wei Shen Lim -** <u>NPNS</u> – 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.