NOT FOR PUBLICATION

COMMISSION ON HUMAN MEDICINES (CHM)

COVID-19 VACCINE SAFETY EXPERT WORKING GROUP

Minutes of the meeting held on **Thursday 28th May 2020** at **10:00** via teleconference

Participants Present

Members

Dr S Misbah (Chair)
Professor I J Douglas
Professor J S Friedland
Sir M Jacobs
Professor S De Lusignan
Professor R Payne
Professor Sir M Pirmohamed
Professor S Quenby
Professor C Robertson
Professor C Semple

Invited Experts

[redacted]
[redacted]
Professor E Miller
Professor A Scott

Visiting Expert

Professor R Shattock

Observers

[redacted]
[redacted]
[redacted]
Professor L Smeeth

[redacted]
[redacted]
[redacted]

Professional Staff of MHRA Present

Supporting Specific Items

Dr P Bryan
Dr K Donegan

MHRA Observers

[redacted]
Dr S Branch
[redacted]
Dr P Myles
Ms N Rose
Mr P Tregunno
Dr J Woolley
[redacted]

Agreed by the Committee and the Chair at its 25/06/2020 meeting as a true and accurate record of proceedings subject to minor amendments.

1. Introduction and Announcement

1.1 The Chair reminded Members, Invited Experts, Visiting Expert and Observers that the papers and proceedings are confidential and should not be disclosed.

The Chair reminded participants to unmute themselves when they wish to speak.

1.2 **Conflict of Interest Policy**

In the pre-deployment phase, the intention is for the remit of the EWG to be non-product specific and focused on methodological/technical activity.

In the post-deployment surveillance phase, the activities will become product-specific (and subject to any relevant conflict of interest)

1.3 The Chair asked all participants to introduce themselves.

2. Terms of Reference and workplan (ToR)

2.1 The Expert Working Group (EWG) noted that at its April 2020 meeting, the Commission on Human Medicines (CHM) endorsed the formation of an Expert Working Group (EWG) on COVID 19 vaccines safety to provide advice on planning and implementation of active safety surveillance.

2.2 Members queried whether evaluation of the efficacy and effectiveness of COVID 19 vaccines are within its remit given that this is essential to the evaluation of risk-benefit balance. It was noted that pre-authorisation evaluation of the efficacy, safety and quality of candidate COVID 19 vaccine was not within the remit of this EWG, but that its activities will complement the work of the other CHM expert advisory group which will advise on product authorisations. The EWG also noted that any emerging evidence of efficacy and effectiveness of the vaccine(s) following vaccine deployment, such as from studies expected to be gathered by Public Health England and other public health authorities, and any data that may be gathered through active surveillance of disease enhancement, will be considered by the EWG as part of the post-deployment phase to inform risk-benefit balance.

2.3 The EWG was informed that MHRA are working actively with PHE and DHSC, and are engaged with the devolved health authorities, in activities around deployment and surveillance of COVID 19 vaccines, and that this engagement across the public health sector will avoid duplication of activities on vaccine surveillance. The activities and outputs of the EWG will also be shared with the Joint Committee on Vaccination and Immunisation.

2.4 The EWG members endorsed the proposed terms of Terms of Reference and proposed workplan, with the addition of advising on any communications

to health professionals and the public during the pre-deployment phase of work. Members also commented that focusing the name of the EWG on 'safety' may not reflect the Terms of Reference and suggested amending the title to "Expert Working Group On COVID-19 Vaccines".

3. Clinical endpoints for COVID-19 vaccine safety surveillance

3.1 The EWG considered a paper outlining a range of clinical conditions as potential endpoints for proactive safety surveillance of COVID 19 vaccines. The EWG agreed that, at present, there are no product-specific serious safety concerns associated with current candidate COVID 19 vaccines for inclusion as endpoints for post-marketing surveillance, but that this will be kept under continual review as evidence emerges from ongoing clinical trials. The EWG also agreed that as COVID 19 disease enhancement is currently a theoretical risk for any COVID 19 vaccine this is an important endpoint that requires active surveillance. The EWG advised that as any potential immune-mediated disease basis for this theoretical risk is unclear, this should be referred to as disease enhancement rather than antibody-dependent disease enhancement. The EWG also considered that as there is currently no information on vaccine-induced immunogenicity or antibody persistence, this endpoint would require long-term follow-up.

3.2 The EWG agreed that there is no specific clinical case definition or biomarkers for possible COVID 19 disease enhancement, and that any such events would be expected to present clinically within the spectrum of severity of COVID-19 disease. As this endpoint has overlap with vaccine effectiveness, the EWG advised that care is needed to differentiate this from a lack of effectiveness, given that 100% vaccine effectiveness in all cohorts is unlikely, as well as any effects of concurrent treatment.

3.3 The EWG endorsed the range of other proposed clinical conditions outlined in the paper for inclusion in active surveillance. The EWG agreed that these should be included not because they are likely, potential or anticipated side effects of any candidate COVID-19 vaccines, but due to past associations with other vaccines, whether causal or not, and conditions that we expect to occur naturally in the absence of vaccination in different population groups. This approach is intended to support both rapid signal detection of potential risks, as well as proactive management of likely coincidental associations and their impact on vaccine confidence.

3.4 The EWG also advised that a range of adverse pregnancy outcomes should be actively monitored if COVID 19 vaccines are recommended in pregnancy but advised that further consideration should be given to defining the proposed endpoints.

3.5 The EWG agreed that although Kawasaki syndrome should be included for active surveillance, further consideration should be given to the relevant case definition and diagnostic coding to identify cases of the paediatric inflammatory multisystem syndrome recently-identified in some COVID 19

patients, as these are not considered to be Kawasaki syndrome and have also been identified in older age groups. It was noted that work was ongoing through the WHO and the British Paediatric Surveillance Unit on a case definition.

3.6 The EWG also recommended that venous thromboembolism should be included in the list.

3.7 The EWG was informed that all of the proposed clinical endpoints will be age-stratified in the methods for active surveillance.

4. Landscape analysis of UK Electronic Healthcare Data Sources for vaccines

4.1 The EWG considered a paper outlining electronic data sources available in the UK which provide data on individual-level vaccine exposure, patient characteristics and potential confounders, and clinical outcomes and which could be used for active safety surveillance.

4.2 The EWG noted that MHRA currently uses the Clinical Research Practice Database (CPRD) routinely in vaccine safety surveillance. As a large proportion of any future COVID 19 is likely to be administered via GP surgeries, the EWG agreed that CPRD will provide a key source of data to support active safety surveillance. The EWG also agreed that Hospital Episode Statistics (HES) will be a key source of safety and noted that MHRA is working in close collaboration with Public Health England (PHE) who have experience vaccine safety surveillance using HES.

4.3 The EWG advised that as the capture of near real-time data to support active safety surveillance will be crucial, it will be important to encourage health professionals to quickly record any vaccine administered in individual electronic health records.

4.4 The EWG also heard that a future COVID 19 vaccination programme could potentially involve novel settings of vaccine administration and considered it important to explore the ability of vaccine exposure to be recorded and rapidly linked to individual electronic health records wherever a vaccine may be given.

4.5 Aside from use of the existing electronic healthcare datasets, the EWG asked whether use of other technology, such as an app, could be considered to gather information directly from patients on vaccine exposure and adverse events. The EWG acknowledged that this form of solicited active surveillance would require careful design but should be considered as an option.

4.6 The EWG agreed that each of the datasets included in the paper will contain relevant data to support active vaccine surveillance and endorsed the proposal to explore these further.

5. Any Other Business

5.1 None.

6. Date and time of future meetings (All meetings will start at 10:00)

Thursday 09 July
Thursday 23 July
Thursday 06 August
Thursday 20 August

The Meeting started at 10:04 and ended at 11:54

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