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

Minutes of the meeting held on **Monday 19th July 2021** at **10:00** via videoconference

Participants Present

Members

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

Apologies

Professor D Goldblatt
Professor H J Lachmann
Professor C Robertson
Professor M Turner
Professor C Weir

Observers

[redacted]
Professor W S Lim
[redacted]

Secretariat

[redacted]

[1] joined during item 3

Professional Staff of MHRA Present

Principal Assessors

Dr J Bonnerjea - LD

Presenters supporting specific items

[redacted] - VRMM
[redacted] - VRMM
[redacted] - VRMM
[redacted] - VRMM
[redacted] - VRMM

MHRA Observers

[redacted] - VRMM
[redacted] - VRMM
[redacted] - VRMM
[redacted] - LD
Dr S Branch - VRMM
[redacted] - VRMM
[redacted] – MHRA Policy
[redacted] - VRMM
[redacted] - VRMM
[redacted] - VRMM
[redacted] – LD – Medical Writer
[redacted] - LD
[redacted] - Comms
Mr P Tregunno - VRMM

[redacted]

19th January 2023

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 Professors Goldblatt, Lachmann, Robertson, Turner and Weir for this meeting.

1.5 The Chair welcomed the following observers:

[redacted] JCVI

[redacted] Public Health England

Professor Wei Shen Lim
Chair of JCVI

[redacted]
Public Health England

[redacted] Public Health Wales

[redacted]
NHS England and NHS Improvement (National)

2. Minutes of the COVID-19 VBR EWG meetings

2.1. Thursday 31 December 2020

2.1.1 The minutes of the meeting were approved as a true and accurate record of the proceedings.

2.2. Sunday 03 January 2021 (HLA Subgroup)

2.2.1 The minutes of the meeting were approved as a true and accurate record of the proceedings.

2.3. Friday 22 January 2021

2.3.1 The minutes of the meeting were approved as a true and accurate record of the proceedings.

2.4. Friday 29 January 2021

2.4.1 The minutes of the meeting were approved as a true and accurate record of the proceedings, subject to the resolution of hidden text to be identified and removed from the document.

2.5. Thursday 04 February 2021

2.5.1 The minutes of the meeting were approved as a true and accurate record of the proceedings.

2.6. Monday 15 February 2021

2.6.1 The minutes of the meeting were approved as a true and accurate record of the proceedings, subject to the resolution of hidden text to be identified and removed from the document and a clearer explanation of item 7.5.

2.7. Thursday 25 February 2021

2.7.1 The minutes of the meeting were approved as a true and accurate record of the proceedings, subject to the resolution of hidden text to be identified and removed from the document.

2.8. Thursday 18 March 2021

2.8.1 The minutes of the meeting were approved as a true and accurate record of the proceedings, subject to the resolution of hidden text to be identified and removed from the document.

3. Pfizer/BioNTech COVID-19 vaccine - Monthly Safety Update

3.1 The EWG were presented with the fourth general safety update for the Pfizer/BioNTech COVID-19 vaccine. The update included a summary of Yellow Card data received in association with Pfizer/BioNTech COVID-19 vaccine (Data lock point 29/06/2021) and updates on safety topics currently under review for this vaccine including observed versus expected analyses conducted by MHRA for the issues of Bell's Palsy, Guillain-Barre syndrome (GBS) and immune thrombocytopenia.

3.2 The EWG heard that up to and including the 29/06/2021, the MHRA had received a total of 86,338 UK reports for the Pfizer/BioNTech COVID-19 vaccine, including both spontaneous Yellow Card reporting and reports from the Yellow Card Vaccine Monitor, and that most of the events reported related to reactogenicity and were in line with the known safety profile of this vaccine.

3.3 The EWG were reminded that the product information for Pfizer/BioNTech COVID-19 vaccine had recently been updated to include warnings on myocarditis and pericarditis and these events remained under close review by the MHRA. Several other safety topics were also currently under close review for Pfizer/BioNTech COVID-19 vaccine including anaphylaxis, thromboembolic events with concurrent thrombocytopenia, menstrual disorders, Bell's Palsy, GBS and immune thrombocytopenia. The EWG were informed that separate reviews of Bell's Palsy, GBS and menstrual disorders in association with COVID-19 vaccines were planned to be considered at upcoming EWG meetings.

3.4 The EWG noted that the Yellow Card reports of suspected adverse reactions with a fatal outcome included reports of deaths in obstetric cases. The EWG were advised that the use of all COVID-19 vaccines during pregnancy and during breastfeeding was kept under close review by MHRA and a paper on this issue would be presented to the EWG at their next meeting.

3.5 The EWG held an initial discussion of the issue of GBS ahead of the separate detailed paper on this topic to be considered at the next EWG meeting. The EWG noted that facial paralyses had been observed as common feature of GBS reported following vaccination with AstraZeneca COVID-19 vaccine and considered that it would be important to look at whether the reports of GBS reported following the Pfizer/BioNTech COVID-19 vaccine had clinically similar features. The EWG also considered that while no signal of GBS has been identified following either the first dose of Pfizer BioNTech COVID-19 vaccine or after the second dose in the older population, it would be important to keep the risk of GBS under close review as second doses of this vaccine were rolled out in the younger population.

3.6 The EWG noted that an MHRA epidemiology study on Bell's Palsy was near completion and would be presented at a EWG meeting shortly. The EWG heard that the results of the study so far were reassuring, particularly in relation to the Pfizer BioNTech COVID-19 vaccine.

3.7 Overall, the EWG advised that while a number of issues were subject to on-going review for Pfizer/BioNTech COVID-19 vaccine, no new issues had been identified in this safety update. The EWG advised that the safety of the Pfizer/BioNTech COVID-19 vaccine should continue to remain under close monitoring by MHRA.

4. Update on myocarditis and pericarditis with the mRNA COVID-19 vaccines

4.1 The EWG were presented with an update on international action that had been taken regarding myo/ pericarditis in association with mRNA COVID-19 vaccines, new international safety data and updated UK epidemiological analyses and Yellow Card data.

4.2 The EWG heard that the EU product information for Pfizer/BioNTech and Moderna COVID-19 vaccines had been updated to include a warning about myo/pericarditis and to list myocarditis and pericarditis as a side-effect. The EU myo/pericarditis wording was similar to the updates made to UK product information for mRNA vaccines. However, there were some differences in terms of the description of the course of myocarditis and pericarditis following vaccination described as 'not different from myocarditis and pericarditis in general' in EU wording and described as 'mild' in UK product information. The EWG heard that a direct healthcare professional letter on myocarditis and pericarditis was also planned in the EU.

4.3 The EWG noted the updated EU/EEA safety data on myocarditis and pericarditis in relation to mRNA and adenoviral COVID-19 vaccines. The EU/EEA reporting rates of myo/pericarditis were 1.6 and 1.9 cases per million doses for Pfizer/BioNTech and Moderna COVID-19 vaccines, respectively. Cases primarily occurred within 14 days after vaccination, more often after the second dose and in younger adult men. The EU/EEA reporting rates of myo/pericarditis were 2.1 per million doses for AstraZeneca COVID-19 vaccine and 1 case in the context of 2 million doses for Janssen COVID-19 vaccine. The EMA concluded that further information was needed to assess whether there was a causal relationship with myo/pericarditis and adenoviral COVID-19 vaccines and had requested further data from the companies on this issue.

4.4 The EWG heard that in Singapore warnings about the risk of myo/pericarditis had been added to mRNA COVID-19 vaccine product information. Further, the Ministry of Health in Singapore had issued precautionary advice recommending that 'adolescents and younger men, who have received any dose of the mRNA COVID-19 vaccines, should avoid any exercise or strenuous physical activity for one week after vaccination'. This advice followed case reports in Singapore of cardiac arrest and myo/pericarditis post COVID-19 vaccination that occurred following strenuous exercise. The EWG also heard that Singapore had recommended that anyone with myo/pericarditis after the first dose should not have mRNA COVID-19 vaccines for a second dose.

4.5 The EWG heard that the US CDC had published a benefit risk analysis of mRNA COVID-19 vaccines and myo/pericarditis which showed that the benefits of vaccination in terms of preventable COVID-19 cases and hospitalisations, ICU admissions and death due to COVID-19 were greater than the number of expected myo/pericarditis cases after vaccination.

4.6 The EWG were presented an updated analysis of SUS hospital data from PHE which included an additional sensitivity analysis to include the term 'pulmonary congestion and hypostasis' which showed a strengthened signal of an increased risk of myocarditis in younger age groups (15-39 years) for the first dose of AstraZeneca vaccine and first and second doses of Pfizer/BioNTech vaccine in the 0–6-day risk window, however these data were based on small numbers of cases.

4.7 The EWG heard that there has been an increase in the number of Yellow Card reports of myo/pericarditis since the last update to the EWG on this issue, particularly for Pfizer/BioNTech COVID-19 vaccine which may, in part, maybe due to recent media attention about this issue. MHRA would continue to closely monitor this issue including presenting a review of sudden death and cardiac events in the next update to be presented at the next EWG meeting.

4.8 The EWG highlighted the importance of close monitoring of reports of myo/pericarditis as second doses of mRNA COVID-19 vaccines were beginning to be rolled out in the younger age group and that it would also be important to closely monitor reports of myo/pericarditis if booster doses of COVID-19 vaccine were to be deployed in the UK.

4.9 The EWG discussed the data from Singapore in relation to reports of myo/pericarditis following mRNA COVID-19 vaccines after strenuous activity. The EWG noted that a similar pattern of events had not been observed in the UK Yellow Card data to date but a question on exercise was now included in the standard follow up form for Yellow Card reports of myo/pericarditis and this issue would be closely monitored.

4.10 The EWG agreed that a time to onset of first 6 to 7 days following vaccination was plausible for the development of myo/pericarditis after mRNA COVID-19 vaccines but highlighted the need for studies into potential mechanisms. The EWG noted that some clinical and

epidemiological studies of myo/pericarditis after vaccination were planned or were ongoing in the UK.

4.11 The EWG discussed the risk of myo/pericarditis after adenoviral COVID-19 vaccines, noting the signal of a possible increased risk after the first dose of AstraZeneca COVID-19 vaccine in the UK hospital data as well as the reporting rates of myo/pericarditis for adenoviral vaccines in the EU/EEA data. MHRA advised that a review of Yellow Card data for AstraZeneca on this issue would be presented to the EWG at their next meeting and the additional data requested by the EMA from AstraZeneca and Janssen on myo/pericarditis would be presented to the EWG when available.

4.12 Overall, the EWG agreed that the benefits and risk of mRNA COVID-19 vaccines remained positive, particularly considering the known high risk of cardiac complications with COVID-19 infection including myo/pericarditis. The EWG advised that this was an important area to keep under close observation especially with AstraZeneca COVID-19 vaccine and second doses of mRNA COVID-19 vaccines in younger populations.

5. Update on COVID-19 Vaccines and risk of thromboembolic events with concurrent thrombocytopenia

5.1 The EWG was presented with the latest data on thromboembolic events with thrombocytopenia associated with the authorised COVID-19 Vaccines up to a data lock point of 14 July 2021.

5.2 The EWG was presented with a summary of a publication of interest – a case report from Spain concerning a patient diagnosed with vaccine-induced immune thrombotic thrombocytopenia (VITT) who developed primary adrenal insufficiency secondary to bilateral adrenal haemorrhagic infarction due to bilateral adrenal vein thrombosis. The EWG agreed that the case reiterated the need for continued vigilance for unusual sites of thrombosis in the setting of VITT.

5.3 The EWG was presented with an overview of the UK case reports associated with the AstraZeneca (AZ) COVID-19 Vaccine. This included the total number of UK cases classified as confirmed, probable or possible (411 cases) as well as summary tables of the 44 reported confirmed, probable and possible UK cases occurring after a second dose.

5.4 The EWG was updated that there have been no new cases concerning patients aged <40 years old who received the AstraZeneca vaccine after the Joint Committee on Vaccination and Immunisation updates on 07 April 2021 (use in <30 years old) and 07 May 2021 (use in <40 years old).

5.5 Data from the weekly COVID-19 safety report published by the Therapeutic Goods Administration (TGA) was summarised for the EWG. Up to 11 July 2021 the TGA reported 83 thrombotic thrombocytopenia cases attributed to AstraZeneca COVID-19 vaccine exposure in Australia. This is a rise from the previously reported 76 cases up to 04 July 2021.

5.6 The UK and foreign cases associated with the Pfizer, Moderna and Janssen COVID-19 vaccines were summarised using the same case definition. There was 1 new UK case and 4 non-UK cases for Pfizer classified as possible. There was no change in the data for Moderna. For Janssen, 6 non-UK cases were reclassified as confirmed after further information on the cases was provided.

5.7 The estimated number of second AstraZeneca COVID-19 vaccine doses administered has increased to 22.8 million whilst the estimated number of first doses has increased by 100,000

since the last data lock point. Estimated case incidence rates for CVST and CVST plus other thromboembolic events were presented by age-stratified 10-year intervals and by gender. The overall incidence rate of CVST plus other TE has remained constant at 14.8 (13.4, 16.4) per million for first/unknown doses and decreased to 2.6 (2.0,3.4) per million first/unknown doses for overall fatal incidence rate. The age-stratified incidence rates associated with second doses were presented and the overall rate increased to 1.9 (1.4, 2.6) per million doses. There were no new fatal cases following a 2nd dose reported since the previous data lock point of 7th July 2021. The case incidence rates per 100,000 patient years following 28 days post-vaccination were also compared for first and second doses. The case incidence rates (per 100,000 patient years) were 15.4 (13.7, 17.3) for the first or unknown doses and 1.6 (1.1, 2.3) for the second doses. The risk estimates were then compared with the expected benefits of vaccine in age subgroups. The reported incidence rates showed no increase since the last data lock point with overlapping 95% confidence intervals, while risk-benefit ratio remained relatively unchanged. Finally, a question on update of benefit-risk analysis was raised. Upon careful consideration of an update of analysis and a consultation with colleagues at PHE, the update will not be undertaken soon as all the assumptions used for benefit-risk analysis based on second wave data remain valid for the Delta variant.

5.8 The EWG then considered the following 3 questions:

5.8.1 Question 1: based on the evidence presented does the EWG consider the benefit-risk balance remains favourable for all patients and for all age groups?

The EWG advised that the overall benefit-risk profile of the AstraZeneca COVID-19 Vaccine remains positive although, depending on the status of COVID-19, its severity and impact on hospitalisation, the benefits of immunisation in individuals aged under 40 years are probably outweighed by the potential risks. The benefit-risk assessment has not changed since it was last reviewed on 12th July 2019.

5.8.2 Question 2: Does the EWG consider there might be an increased risk for the second dose of the vaccine?

The EWG advised that the emerging data on the risk of thromboembolic events occurring with thrombocytopenia following second doses remains reassuring. The MHRA should continue to monitor second dose cases closely, particularly as younger patients continue to receive their booster immunisations.

5.8.3 Question 3: Does the EWG consider there is any need for action with regards to the Pfizer, Moderna or Janssen vaccines in relation to this potential risk?

Based on available data, the risk associated with the Pfizer and Moderna COVID-19 vaccines appears lower than that associated with the AstraZeneca COVID-19 Vaccine. This risk should be monitored and there is no need for regulatory action. Events associated with other COVID-19 vaccines should continue to be closely monitored.

6. Capillary Leak Syndrome and COVID-19 vaccine Janssen

6.1 The EWG was presented with a paper on the risk of capillary leak syndrome (CLS) and COVID-19 vaccine Janssen. The EWG was informed that the Marketing Authorisation Holder (MAH) had requested to include CLS in the Product Information (PI) as an adverse event and to include a contraindication in patients with a prior history of CLS, following updates to include these for the AstraZeneca COVID-19 vaccine (PI), another adenovirus-based vaccine. The MAH also proposed a direct healthcare professional communication (DHPC) letter to communicate the proposed updates.

6.2 The EWG was presented with the worldwide data on CLS for COVID-19 vaccine Janssen. A total of 3 cases of CLS had been identified, with two of the cases reporting a fatal outcome and one case having a prior history of CLS. The EWG noted the similarities in the cases with the ones seen with the AstraZeneca vaccine. The EWG considered that the available evidence supported the addition of CLS as an adverse event in the PI and for a prior history of CLS to be included as a contraindication for the Janssen COVID-19 vaccine.

6.3 The EWG also considered the MAH proposal of a DHPC letter. The EWG considered that as COVID-19 vaccine Janssen is not currently used in the UK, there was not a benefit to a DHPC letter at this time. Communication of the contraindication and risk of CLS would be more beneficial just before the vaccine begins to be used in the UK.

7. Verbal Update: Plans for epidemiological investigation of menstrual disorders

7.1 The EWG were presented with the proposed strategy for capturing further data on the incidence and nature of menstrual disorders following COVID-19 vaccinations including the strengths and limitations of a number of different data sources.

7.2 The EWG noted the numerous challenges with regards to the conduct and interpretation of epidemiological analyses regarding the risk of menstrual disorders.

7.3 The EWG highlighted the need to better understand the wider impact of the pandemic and COVID-19 infection on menstrual cycles. The use of longitudinal data from menstrual cycle tracking apps could be useful here although such data have rarely been used in research and will, like other data sources, be subject to bias.

7.4 Overall, the EWG supported the strategy but advised that the capture of robust data that could be used to conclude on a causal association with COVID-19 vaccinations will be extremely challenging. However, they agreed that there was a clear need to look at other data sources to understand what data they could provide to further understand absolute risk and the duration and severity of menstrual changes.

8. Any Other Business

None.

9. Date and time of next meeting

The next scheduled meeting is to take place **on Friday 23rd July** at **10.30am**.

The Meeting today started at 10:01 and ended at 12:01.

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

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.

Observers

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.

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

Dr Mary Ramsay - Other relevant interests 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.