Royal Society / Academy of Medical Sciences study on pandemic influenza

– Chiron Vaccines' submission of evidence -

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As one of the world's leading producers of influenza vaccines, Chiron welcomes the Royal Society / Academy of Medical Sciences' review of current preparations against the threat of pandemic influenza, and is grateful for this opportunity to submit evidence to the study's distinguished panel of experts.

BACKGROUND

Vaccination is generally accepted as offering the best method for protecting the general population against an influenza pandemic. Nevertheless, vaccination has limitations in the pandemic application:

1) DOSE OUTPUT - Total dose output from industry would be insufficient to meet global pandemic demand, hence some countries will be undersupplied with pandemic vaccine.

2) TIME TO SUPPLY- Even in territories where full supply may be available, the several month production lead time will cause delay in getting vaccines to the market when a pandemic emerges and may well result in incomplete vaccination during the first wave of the pandemic.

3) VACCINE EFFICACY - Efficacy cannot be tested or fully predicted against an as yet unknown strain.

DOSE OUTPUT & TIME TO SUPPLY

As has been highlighted previously by the vaccine industry, it is not practicable to build significant additional surge production capacity for use only in the event of a pandemic, which may occur only every few decades. To establish sufficient capacity to be available in the event of a pandemic a number of steps must be taken:

A) Increased seasonal flu vaccination – increasing 'normal' vaccination rates is essential to encourage the development of additional production capacity. Currently only 22% of the total EU population receives annual flu vaccination; in the US this exceeds 30% and CDC plans to increase this to 50% by 2010. In addition, discussions are ongoing in the US regarding the potential of universal vaccination (as is already the case in Ontario).

B) Dose sparing - the use of adjuvants may reduce the antigen dose required, thereby allowing the production of more doses of monovalent pandemic vaccine from existing manufacturing capacity. Unfortunately, recent experience with H5N1 shows that 'stretching' existing capacity may be challenging to achieve, for several reasons:

- Reduced production yield compared with seasonal strains (H5N1 yield is currently markedly lower that that achieved with seasonal strains) - it is critical to assure a robust output of pandemic vaccines that a high yielding seed virus and test reagents are made available to manufacturers as soon as possible after a pandemic declaration. Resources must be allocated to NIBSC and other centres to achieve this.

- Potential requirement for increased antigen dose compared with seasonal vaccine - recent clinical studies have shown that compared with the 15ug antigen dose used against each seasonal strain, to achieve an acceptable immunogenic response to H5N1, significantly higher doses were required in some studies: up to 90ug of unadjuvanted vaccine and 30ug for an alum adjuvanted vaccine. Further clinical studies are currently in progress, including those exploring the use of MF59 adjuvant, to examine the potential to achieve responses immune responses at lower antigen doses. Industry is also investing in the development of potent adjuvantation systems and longer term in novel antigen approaches. Resources must be made available for this important research priority.

C) Pandemic Pre-vaccination - Discussion has begun in a number of forums regarding the possibility of pre-vaccinating the population, or sub-populations, against a potential pandemic strain. These discussions include the possibility of utilizing current strategic ("emergency") stockpiles prior to shelf-life expiry, as well as producing vaccine for regular preemptive vaccination campaigns against strain(s) of concern. From the perspective of producing sufficient vaccine supply against a pandemic strain this makes good sense, for the following reasons:

- It spreads pandemic vaccine production across many years, rather than requiring significant surge capacity at a single point in time. Conceptually this approach would allow industry to respond in a more effective manner with consistent production of pandemic vaccines and assure a broader distribution amongst the global population of a scarce resource.

- It eases the delay in supply following pandemic declaration; populations would be protected to some level at the outset of the pandemic, assuming the pandemic strain is related to that used in previous immunization campaigns, or that novel technologies such as adjuvanted vaccines provide cross protection.

While these potential strategies have an empirical logic, Chiron believes that they should be pursued based on robust scientific data. Chiron believes these data are not currently in place, and that public-private partnership funding should be devoted to establishing the necessary clinical evidence upon which to base policy development. Studies with H5N1 vaccine currently ongoing should provide a preliminary basis for this work, but additional research will be required to definitively provide global governments with the tools for adoption of this policy.

D) Single dose strategies – Current scientific evidence indicates a probable requirement for 2 doses of pandemic vaccine, rather than one for seasonal vaccines, to provide protective levels of antibody. This is likely because vaccinees will be naïve to a pandemic strain. However, it is clearly logical that to not only stretch the use of existing capacity, but also reduce the significant potential logistical delays and costs of any pandemic vaccination programme, research must be undertaken into strategies to provide adequate immune responses following a single vaccine dose.

Chiron believes that there is not currently sufficient scientific data in this area upon which to base a robust vaccination strategy. Therefore, funding should be focused on the development of potent vaccines requiring only one dose. The use of adjuvants may play a key role in this endeavour, and resources should be allocated to this field of research. Chiron also believes that the preemptive vaccination policy development should link closely with investigation of single-dose strategies, once the scientific basis for each of these approaches has been established.

INCREASED VACCINE EFFICACY

It is important that pandemic vaccines are as effective as possible, particularly if they are to be stockpiled in advance or used in pre-vaccination programmes, where there is the potential that the actual pandemic strain does not completely match the strain incorporated into the vaccine. In addition, there is a key requirement for long lasting protection. The use of adjuvants offering high levels of immune response, long term antibody persistence and cross strain protection may offer this efficacy potential. Funding should be made available to support research into these key areas.

CONCLUSION

The impact of an influenza pandemic is potentially devastating in both social and economic terms, even in developed countries like the UK. Aside from the personal tragedy caused by death and morbidity, the direct healthcare impacts (GP visits, hospitalisations, mortality) can be costed in billions of pounds, and productivity impacts in percentage points of GDP. These impacts can be significantly reduced by timely and robust vaccination of the population, for comparatively modest costs. By supporting the research and actions outlined above, public-private partnerships with industry and government working together can help prevent a repeat of the catastrophic 1918-1919 pandemic.