



## QUESTIONS ON COVID- 19 VACCINE AND DELIVERY OF A NATIONAL VACCINATION PROGRAMME

The Academy is completely supportive of the concept of a new national vaccination programme to help tackle the COVID-19 pandemic.

However, the announcement of a proven vaccine and the start of any implementation programme will generate a deluge of questions from the public, the media and healthcare professionals.

It is essential that as far as is possible there are answers to all these questions known and readily available at the time the vaccine is launched. Without this and the ability for Government, the NHS and healthcare professionals to provide clear and consistent messaging there is a real danger of the programme coming into disrepute very quickly and therefore failing to achieve the desired impact.

The Academy has asked its member organisations what questions they and clinicians on the ground would need to be able to answer to ensure their own and their patients' confidence in the process. These are not going to be a definitive list of issues and new and specific questions will inevitably arise once any vaccine is announced and a programme underway.

We have little doubt that the majority if not all of these issues will have already been considered by those involved in the planning for a vaccination programme and this is not intended to call in doubt that expertise. It is intended as a helpful external "belt and braces" exercise on behalf of the clinical community.

Attached as Annex A is a more detailed submission from the Faculty of Pharmaceutical Medicine.

The Academy is happy to facilitate any briefing or engagement with medical royal colleges

### 1. Clinical issues

- What are the specific vaccines for UK use? Live attenuated/deactivated?
- What are the differences between particular vaccines and why choose the one(s) being delivered over others?
- What is the real data on expected efficacy rate?
- How many doses will be required and at what intervals?
- Are there any known or anticipated side effects with frequency data to allow for planning of staff delivery and honest conversations with public?
- Impact/suitability of particular groups e.g. children, pregnant women, religious groups
- Interaction with other medications conditions

- Do we have fool proof electronic systems, linked to NHS records, for recording who has been vaccinated, with what vaccine, by whom and where?
- Will there be a certificate of immunisation/immunity issued to recipients at point of administration?
- How will safety be monitored and how will we link vaccine batches to individual members of the public
- How long is the vaccine effective?

## **2. Delivery**

- Will the vaccine strategy be UK wide?
- What is the prioritisation of recipients for vaccination?
- Who will be excluded from NHS vaccination and will they be able to obtain it privately?
- Logistical arrangements – expectations on primary care, secondary care?
- Who will call the public forward for vaccination, how will they be notified?
- Will it be one or two stage process?
- Are there opportunities to utilise other healthcare contacts e.g. sexual and reproductive health clinics to deliver vaccinations?
- Which staff will be authorised to deliver the vaccine?
- What are the training requirements/arrangements? Supervision?
- Patients who are shielding – Prioritisation, suitability and delivery?
- Who will vaccinate those who cannot leave home?
- Will vaccine recipients be enrolled onto a registry which then follows their progress over time?

## **3. NHS staff**

- Expectations on NHS staff vaccination - timescale, handling of dissenters
- Prioritisation – which staff should receive it first? Work location? Disease prevalence?
- Staggering delivery in case of adverse reactions causing absence. Is it factored in and honesty about expectations of ADRs?
- Messaging to health care staff – who will lead this? – Suggest honest, data led approach – do not try to hide any truths

## **4. Other**

- Presumably there will be a major communications/publicity campaign for both public and health care professionals – let us help you avoid bear traps?
- Factsheet for HCPs to answer key questions – see above, more scientific based than public info but both must be totally honest (scientists will be lined up to speak both against and for any vaccine so any attempt to hide facts will quickly fail)
- Countering anti-vaxers
- Vaccine “passports” – are they happening? If so, what format & timescale? Is this a global or UK decision and thus will they have international validity?
- As the vaccine will not (entirely) prevent infection, what of the existing social restrictions would be maintained until widespread coverage is attained?

## FACULTY OF PHARMACEUTICAL MEDICINE SUBMISSION

### ***General comments concerning ongoing vaccine trials***

The phase III trials for the front runner vaccines are not powered to demonstrate a reduction in hospitalisations or deaths from COVID-19 and have set a low event rate expectation (150-160 events) in terms of any symptomatic disease or sampling for asymptomatic infection rates. Additionally, the presumptions in the statistical plans are at best 50% effectiveness for reducing disease incidence with a lower bound of 30%. This reflects in part the potentially low community attack rate (1-2%) but also sets a low bar for effectiveness, limiting the extent to which vaccination might impact healthcare usage/personal risk in the face of an ongoing surge of infection.

It is therefore important that the anticipated impact of the vaccine strategy adopted is made clear to clinicians, so they can properly address potential recipients' questions on an individual as well as population basis. For example, the information reviewed and basis for MHRA approval for clinical use of the vaccine and impact modelling for the strategy recommended by the Joint Committee on Vaccination and Immunisation could be made available to healthcare providers.

The N included in any one vaccine trial is insufficient to exclude risk of vaccine enhanced disease. In addition, the duration of follow up (at least 2 months post course completion with an unknown proportion of subjects followed for longer time periods), is potentially insufficient to make an informed judgement concerning vaccine scheduling for different vaccines and modalities in terms of the need for repeat vaccination after completion of the first course. These aspects need to be addressed prospectively: for example, an 'overarching' protocol enabling the pooling of data across studies of different vaccines might enable the relative risk of vaccine enhanced disease to be assessed. In addition, a plan to enable understanding of timing of infection/ disease after use of different vaccines in practice should be put in place to address the issue of potential need for more than annual scheduling of booster shots (suggested by some of the recent data on immune response post disease). Further comments and questions on this follow.

Although some companies have published their data on the impact of pre-existing immunity to the vaccine vector – notably this may be as high as 80% or more of the adult population for Ad5 vectors and high levels of antibody significantly reduced immune response to the SARS-CoV-2 constructs included in these vectors – the potential need to keep giving repeated boosters might result in eventual negation of effect for such vaccines at some point. It is suggested that a biobank be established to enable this to be prospectively investigated. Is this possibility being discussed?

### ***General questions about the implementation and roll-out of a vaccine***

#### **Delivery strategy**

1. Should “everyone” be vaccinated to support a type of “herd immunity” or should vaccination be focussed on mitigation of serious illness and death and therefore potentially more for persons at higher risk? If the latter, what minimum vaccine efficacy will be

required for this to be effective? If the former, are assumptions being made for population coverage targets for each level of vaccine efficacy demonstrated in Phase III, and how long each will take to reach?

2. Although recognising the devolved nature of healthcare in the UK, it seems reasonable to propose that any vaccine strategy is uniform across all four nations of the UK, as it would be extremely difficult to justify a different strategy in England compared to that adopted in Scotland, Wales or Northern Ireland. What will be the strategy for this?
3. On prioritisation of recipients, we understand that healthcare and essential service workers followed by the most clinically vulnerable are at the head of the list. Is a differential approach in terms of logistics being planned for other vulnerable populations? Is the definition of higher risk going to be that which PHE/NHS have been using to date, or will they broaden it to others? Depending on the level of immunity provided this is a key question to understand how any social restrictions are imposed and relaxed for various groups (also see Q8). What the immunity provides (again by age, gender and ethnic group) will be critical to understand as to how the population response is further tailored as a result.
4. Getting the vaccine to patients who have been shielding may be a challenge. How will this be logistically managed?
5. With potentially the parallel roll out of seasonal flu vaccination as well as regular paediatric schedules, will the real possibility of vaccine / immune interference need to be considered in scheduling and is it likely to be different for different SARS-CoV-2 vaccines?
6. What other enabling supplies (sterile disposable syringes etc.) and activities (e.g. public health information programmes) are being put in place that may otherwise be rate limiting, so as not to limit roll out of a vaccine unnecessarily? How will educational materials be managed for a vaccine programme, for health care professionals and patients?
7. Delivery capacity will be key. Based on the need for roll out and its speed and priority, is there a view on co-opting paramedical staff and other medical and healthcare professionals who will be licensed to deliver vaccination, over and above the recently consulted upon proposals?

### **Wider implications**

8. If, in the scenario that the vaccine does not (entirely) prevent infection, but could prevent or reduce illness or serious complications in some people, what of the existing social restrictions would be maintained until widespread coverage is attained (vaccinated individuals with an immune response could be infectious to non-vaccinated people who will remain at higher risk)? How will ongoing population efficacy of the vaccine be monitored?
9. If the vaccine provides complete or very high degrees of immunity, are immunity passports being considered? If so, this should depend upon the extent of immunity provided and at what point sufficient population immunity is reached to keep the spread low enough to reduce infection rates. This is an important question to understand roll out, interim and final

targets and the potential relaxation of societal restrictions for different groups with various risk levels at different times, that will be allowed at each stage.

10. Will vaccinated individuals be encouraged to resume in person clinic visits for clinical trials, outpatient clinics and treatments, and for short / day case procedures? How will each be managed with social distancing, scheduling and staffing?
11. Public acceptance is vital. Is there a plan to identify specific issues of concern that may reduce uptake and so effectively address public anxiety? The special requirements of COVID-19 campaign are likely to go beyond the NICE guidance - <https://www.nice.org.uk/guidance/ng103>. Have the requirements for a concerted national publicity campaign been considered? Have the organisational issues for early communication and increased delegation to local bodies been considered?

#### **Follow-up and monitoring**

12. Will vaccine recipients be enrolled onto a registry which then follows their progress over time? This could be used to establish at the very least whether there is any waning of protection or change in severity of illness among recipients as well as any other later onset vaccination effects – e.g. potential demyelinating events (GBS/transverse myelitis), narcolepsy etc which were observed in the past with influenza vaccines but only came to light post approval. It would be important that the type and batch number of the vaccine administered be recorded in the data collected as this would enable ongoing review of the risk benefit for each vaccine type used in the program. How will the post administration observation period for immediate adverse effects be organised and managed logistically? Will people with prior proven COVID-19 infection also be vaccinated and their immune response followed up?

#### **Questions relating more directly to pharmaceutical medicine**

13. There is a real challenge for communicating and implementing a clear approach on the impact of the first approved vaccine on *other ongoing* COVID vaccine studies. Are there plans in place for this? There is a risk their effect will be diluted as people do not participate in studies and the placebo (and active) groups are confounded by roll out of the approved vaccine. How will this scenario be managed? Will studies into other vaccines continue and remain blinded? If not, how will the ongoing question of loss of effect and requirement for repeat scheduling be addressed?
14. If recruitment to placebo arms in vaccine studies becomes impacted, will guidance be developed on pooled placebo assessments and non-inferiority studies between active vaccines, to minimise the impact and possible futility of ongoing studies?
15. Receipt of vaccination may impact the outcomes of trials of COVID-19 therapeutics and may necessitate adjustment of sample size to compensate for changes in disease severity and protection from disease offered by vaccination; this will need to be prospectively assessed and adjustments made in ongoing clinical trials. e.g. will vaccination be an exclusion to entry into clinical trials of other medicines? Will vaccination be a requirement for entry into clinical trials of other medicines?

16. For non COVID-19 studies, guidance on e.g. medication / IMP interaction and the impact of differential assessment tools and comparability will be needed. If the vaccine is introduced via an EAMS, it may not be considered a licensed medicine, so any subject that has had the vaccine might be excluded from participation in other clinical trials. Will only immunised patients be able to participate in studies? Will trials of other pharmaceuticals be amended to permit inclusion of subjects that have received COVID-19 vaccination under a national vaccination scheme?
17. Will COVID-19 vaccines be advertised to healthcare professionals by companies?
18. Will vaccine supply be solely by government control or will companies be allowed to sell vaccine for private prescription and use?

***About FPM***

The Faculty of Pharmaceutical Medicine is a charity and professional membership body on a mission to advance the science and practice of pharmaceutical medicine.

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