

# VTF RECOMMENDATIONS

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<b>RECOMMENDATIONS NOT FOR PUBLICATION</b>
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It is clear from the COVID19 pandemic that the UK needs to be part of a rapid response system to discover and develop vaccines for novel threats and ensure it has a resilient supply of vaccines and antibodies for infectious threats new and old.

We need to act quickly to prevent pandemics occurring so the UK needs a permanent ecosystem for rapidly developing, manufacturing and supplying vaccines for future pandemics, ensuring domestic resilience and security, while also creating long term economic prosperity.

To cement the UK's role as a global leader for pandemic response, we need a diverse, informed infrastructure for surveillance of adverse events, flexible capacity for manufacturing and testing vaccines and a global funding facility for purchasing and distributing vaccines internationally.

For vaccines to play an effective part of pandemic recovery and preparedness, they must be available quickly and be manufacturable at scale. The Vaccines Taskforce has demonstrated its contribution to the current pandemic recovery, and the lessons learned should be applied to our future preparedness.

We set out below a series of recommendations that will ensure the UK is able to address its capability gaps and develop our system resilience and security by maintaining the legacy of the Vaccines Taskforce and to deliver economic growth and the levelling up agenda alongside long term prosperity to the UK.

## 1. Creation of a National Vaccines Agency<sup>1</sup>

The experience of the VTF has demonstrated that pandemic response and readiness requires a wide range of stakeholders, both domestic and international, public and private, to come together to deliver effectively. The heightened pace of work the VTF generated and delivered because of COVID19 will be difficult to replicate in peacetime, but it is clear that having the ability to draw together networks is crucial to pandemic preparedness.

The VTF recommends the creation of a new executive agency within BEIS as its successor, as the central body responsible for co-ordination of industrial and public sector assets, as well maintaining the relationship between the UK's vaccines industrial base and HMG. The

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<sup>1</sup> A separate paper describes the structural and governance options for this proposed new agency

proposed National Vaccines Agency (NVA) would report into BEIS and work closely with all relevant government departments and public bodies.

## Scope

The NVA's remit would include vaccine scale-up and manufacturing, including of supply chain readiness, tech transfer & stockpiling, oversight of the UK's clinical development capability including immunological profiling and human challenge models as well as attracting and supporting the development of innovative new vaccines.

It would also monitor and relay current threat assessment of novel diseases to industrial partners, working in partnership with cross-government functions on horizon-scanning and intelligence.

On innovation, it would inform and influence UKRI budget and asset development to ensure academic base and innovation support targets the needs of vaccine development pandemic preparedness.

Primarily, the new agency would own and oversee the implementation of the recommendations set out in this report.

## Governance

An independent, industrially experienced Chairman and board should be established to bring together the work of the various strands of vaccine activities that will define the UK as a global leader in vaccine development and manufacturing.

### Recommendation 1

\*Create a National Vaccines Agency (ALB executive agency). Attachment explores further options.

## 2. c

Many of the vaccines being developed to address the current pandemic are at the cutting edge of science. When it comes to distribution and delivery to patients however, they rely on traditional methods using vials and syringes that are slow to distribute and deliver to patients at scale, involve complex supply chains and specialist storage and distribution conditions. Investment in vaccine production is often weighted towards discovery, and more needs to be done on the industrialisation and customer-facing end.

Establishing a National Capability for Formulation and Delivery would bring those cutting-edge developments in vaccine formulation, delivery, process development, and scale-up together. The new centre would draw on existing resources in the current UK medicines manufacturing

innovation infrastructure, consolidating the expertise of VMIC, CG-MIC and the Centre for Process Innovation, and co-ordinate delivery across the UK.

Its focus would be on developing new modes of administering vaccines, focusing on innovating delivery through the mouth (oral), skin (transdermal or intra-dermal) or nose (intra-nasal), and tackle the barriers that exist in the market which prevent the scale up and commercialisation of those novel vaccine formulation technologies – innovation that is crucial to build on if the UK seeks to be a global leader in pandemic preparedness [hold for line on domestic vaccine access].

## **Recommendation 2**

Establish a National Centre for Formulation and Delivery to bring together capabilities across vaccine formulation, delivery, process development, and scale-up.

### **3. Enhance UK Clinical Trial Capability**

A function which the National Vaccines Agency would support would be enhancing the clinical trial capability in the UK. This would leave the UK better prepared to incorporate vaccines in its pandemic response in future by improving the speed of vaccine development while maintaining quality. These recommendations outlined below are designed to achieve this. Additionally, these recommendations would reinforce confidence in the UK clinical trial capability, to attract future investment from private companies onshore which strengthens HMG's position in the face of a future pandemic.

There are several stages to vaccine development. Initially a vaccine candidate is identified through research. This candidate then enters pre-clinical trials which examine safety and dose in animal models. After a candidate successfully completes these pre-clinical trials, it then undergoes four clinical phases (to which these recommendations pertain). Phase I checks the safety in humans in a small trial population, before phase II where the safety of the candidate is explored in a larger trial population. Phase III again includes a larger population than phase II, but this looks not just at the safety of the candidate vaccine, but also at the efficacy at treating the disease for which it was designed.

After a vaccine successfully completes the first three phases of clinical trials it can then be licenced and placed on the market. The Medicines and Healthcare products Regulatory Agency (MHRA) provides the licencing and marketing authorisation in the UK. The final phase, phase IV, is a long-term surveillance of the vaccine in real world scenarios, to examine long term effects.

In responding to COVID19 the VTF has identified points at which improvements in these clinical trial phases can be introduced so that going forward HMG and the UK are better prepared for the development of vaccine candidates for novel infectious diseases.

#### **Clinical Immunology Network**

The first improvement to enhance clinical trial capacity in the UK going forward would be to establish a Clinical Immunology Network (CIM). This would align and integrate studies on natural immunity with vaccine clinical trials, by using standardised assays. This allows the data to be directly compared between trials so that the UK can develop a broader understanding of effective immune responses. The CIM can then ensure that preclinical and clinical studies involve testing of the critical immunity components used in industrialised validated assays.

The network would include organisations and stakeholders from academia, clinical, life sciences industry and government, and their expertise to profile emerging new vaccines, create high capacity validated assay formats that can be used in preclinical development and clinical vaccine trials.

This enhances the clinical trial capability of the UK by generating rich immunological data that we do not currently have. This data, in turn would help improve the speed and quality of the clinical trial phases by increasing our understanding of immunology. It would lead the UK better prepared to develop novel vaccine candidates in the face of a future pandemic.

### **Recommendation 3.1**

Formalise a network between partner organisations to support research and development in clinical immunology, to support increased rich immunological data generation

## **Human Challenge Trial Centre of Excellence**

Human challenge trials are those in which volunteers (who have been given the trial vaccine or a placebo) are intentionally exposed to the infectious agent within a controlled research environment. The UK is currently home to the leading human challenge academic research, and thousands of volunteers have been through human challenge models. Currently the UK is the only country to set up a human challenge model for COVID19.

In this respect the UK has the experience to lead the world in this field. However, the current UK human challenge capacity is limited. It is for this reason that the VTF recommends a Human Challenge Centre of Excellence (HCCE), so that the UK may build on the capacity currently in place and continue to lead in this regard.

The benefits of establishing a HCCE would have for improving UK government's preparedness for future pandemics are multifaceted. By undertaking a human challenge model in phase III clinical trials (when researchers are examining the efficacy of the vaccine) the timescale can be significantly accelerated, as researchers are not waiting for trial subjects to be exposed to the disease naturally in the population. As a result decisions based on efficacy are not dependent on infection levels and transmission rates within the population and it becomes easier to draw direct comparisons between candidate vaccines. In addition, it allows for researcher to control the entire model and allows them to collect additional data that would not be possible if infection were acquired in the wider population. A HCCE would therefore allow for vaccine development to be accelerated without compromising the safety of the

vaccines developed, which would leave the UK better prepared for vaccine development in the future. In addition, there has been global interest the human challenge model being employed against COVID19 and launching an HCCE would capitalise on this. It would encourage companies developing vaccines in response to a future pandemic to run their phase III clinical trials in the UK, helping to encourage pharmaceutical development onshore. This would help the UK to prosper, and leave HMG better prepared in a future pandemic.

### **Recommendation 3.2**

Launch a Human Challenge Study Centre of Excellence to further the UK's clinical trial capability for respiratory infections and diseases

### **Vaccine National Research Registry**

In response to COVID19 the UK National Institute for Health Research (NIHR) established a COVID19 vaccine research registry through the NHS. This was to allow people to register their willingness to participate in the different vaccine clinical trials within the UK. This has allowed clinical researchers to easily enrol eligible volunteers in their trials. Going forward maintaining this registry for future vaccine trials and in future pandemics would enhance clinical trial capability by simplifying the process by which volunteers are enrolled in trials. This would help the UK government in a future pandemic as it would allow for volunteers to be rapidly mobilised as soon as candidate vaccines reached clinical trials.

Of the 350,000 registered as part of the COVID19 effort, 94% expressed willingness to be contacted for non-COVID19 research. By regularly engaging with this registry, keeping it up-to-date and expanding upon it, HMG can create a valuable resource to improve clinical trial capability and aid in the development of novel vaccine candidates in future pandemic responses. Moreover it would be a huge asset for the UK clinical research environment and a unique selling point (USP) to attract clinical research investment from the life sciences industry in the UK

### **Recommendation 3.3**

Expand the UK vaccine registry capacity, refine the registry by enabling the linking of NHS datasets of consenting individuals to the vaccine register, maintain active communications with registrants and the public and enhance researcher access.

## **4. Enhance UK Manufacturing Capability, Responsiveness and Breadth**

After a vaccine candidate has successfully been licenced, it is then able to be manufactured at scale and placed on the market. For HMG to be ready to include these newly licensed

vaccines in response to a future pandemic, it is necessary to ensure that manufacturing capability is sufficient to produce a vaccine at scale.

Over the past ten years there has been a significant decline in pharmaceutical manufacturing within the UK, which has meant that there is significant reliance on international supply for manufacturing. COVID19 has shown us that a pandemic can disrupt supply chains and therefore these recommendations attempt to prepare for this by suggesting points at which manufacturing can be undertaken within the UK. This would improve readiness in the event of a novel pandemic.

In addition to vaccines and antibodies for COVID19, we also need to consider:

- Ongoing stockpiles of flu pandemic vaccines (H1N1)
- Potential stockpiles of adjuvants
- New pandemic vaccines

These recommendations seek to enhance our manufacturing capability, proposing new manufacturing methods and improvements across the production process, whilst also ensuring the UK is equipped to manufacture and surge capacity as part of its preparedness strategy. Key for the UK is to retain optionality to develop new pandemic vaccines as rapidly as possible, but also to develop vaccines with optimal characteristics (stable, scalable, needle-free etc). Also which, if any of the vaccine formats can be combined with flu. We don't yet know which vaccine modality is best suited to oral, transdermal or inhaled deliver hence the recommendation to maintain flexibility to manufacture viral vectored vaccines, mRNA vaccines, protein adjuvant vaccines and whole inactivated virus vaccines.

These recommendations seek to enhance our manufacturing capability ( including both Contract Development and Manufacturing Organisations CDMOs and nationally supported infrastructure) proposing new manufacturing methods and improvements across the production process, whilst also ensuring the UK is equipped to manufacture and surge capacity as part of its preparedness strategy. For this strategy to work it is essential that partnerships are encouraged and created to enable CDMOs and Nationally supported facilities to work in harmony in pandemic and non-pandemic times, creating a vibrant ecosystem for health and economic benefit for the UK.

### **Protein-based Vaccines**

Plant based manufacture of protein antigens is the quickest and most reliable way of generating Good Manufacturing Practice (GMP) protein for protein-subunit based adjuvanted vaccines. For example, advanced plant-based technology can produce Good Manufacturing Practice (GMP) protein in less than three months after a pandemic viral sequence has been defined.

The UK has no rapid protein manufacturing capability in the UK for protein-based vaccines, and so the VTF recommends the use of nimble existing tobacco plant technology to manufacture adjuvanted protein-based vaccines. This would allow for the UK to produce protein-based vaccines on a hugely accelerated timescale, allowing for successful candidate

vaccines to be manufactured at a large scale, and distributed quickly. In addition this manufacturing process would not be subject to international supply chain disturbances, ensuring the UK is better prepared for a future pandemic.

#### **Recommendation 4.1**

The UK should invest in plant-based manufacture of protein antigens to quickly and reliably generate the protein for protein-subunit based adjuvanted vaccines.

### **mRNA Vaccine capability**

Early Phase 3 data from Pfizer/BioNTech and Moderna has been hugely encouraging, suggesting a broadly consistent safety and efficacy profile across all evaluated subgroups. The VTF believes that securing access to mRNA vaccines is an important capability for the UK as part of its pandemic preparedness, given the speed to develop this flexible vaccine format. The VTF has acquired vaccine doses from each of BioNTech/Pfizer and Moderna, but neither of them has chosen to manufacture in the UK, nor appear likely to in the future. The VTF has been funding initial clinical trials of Imperial College's self-amplifying RNA (saRNA) and data is awaited. It will be important to develop improved formulations that stabilise the mRNA vaccines to reduce the complexity of the cold chain.

The UK is fortunate to have leading companies in RNA manufacture, both biological plasmids and synthetic DNA. With investment, both could be formulated for intranasal or intradermal use, which would be highly attractive for mass deployment,

Through VTF's funding of the Centre for Process Innovation, the UK now has a GMP mRNA manufacturing scale up and process development capability that can be used for manufacturing of a mRNA vaccines. There are several UK companies with state-of-the art DNA production which could provide important technologies for future mRNA vaccines and opportunities to collaborate should be explored. CPI have demonstrated capability in the formulation of RNA in lipid nano particles which allows intracellular delivery of the RNA and is a critical and an increasingly important delivery mechanism in gene therapy as an alternative to viral vectors.

**Recommendation 4.2:** Explore potential opportunities to partner with the most promising mRNA based companies, academics and others to provide state-of-the-art mRNA capability to address future pandemics.

### **Domestic Antibody Production**

There are half a million immunocompromised patients in the UK, for whom a vaccine will not be efficacious. In addition, there may be front line and military workers who need immediate protection. A neutralising antibody cocktail may be able to provide short term prophylactic protection to these people. To ensure the UK is better prepared to face the next pandemic therefore, the VTF recommends investing in domestic antibody production so that supply is

less likely to be disturbed and vulnerable patients and frontline workers are protected. This would also ensure that the UK can protect individuals before a successful vaccine is developed, which would ensure that HMG is better prepared in a future pandemic.

The UK should develop the capacity to manufacture neutralising antibodies at scale by investing in and building bulk antibody manufacturing capability. It could do this by focusing on advancing technology and facilitating production, working in partnership with the private sector such as antibody developers and CDMO/manufacturers.

#### **Recommendation 4.3**

Establishing bulk antibody manufacturing capability to ensure capacity to manufacture sufficient neutralising antibodies to meet needs of UK's immunosuppressed population and frontline workers.

### **Securing the Supply Chain**

Improving the supply chains that support a vaccine manufacturing process has been a priority for many years as part of pandemic preparedness. COVID19 has demonstrated how challenging international supply chains can be, and the VTF's response during this crisis has also shown the importance of maintaining relationships with global partners to overcome supply chain risks.

The process for producing a vaccine has multiple touchpoints, both domestic and international. As the UK develops its capability to produce a vaccine from end to end, it should also develop a strategy to understand and respond to global interdependencies and supply chain crunch points.

The VTF recommends assessing the UK's vaccines supply chain capability and building a mechanism which monitors and quality assures the resilience of global supply chains, as overseen by the National Vaccines Agency.

A clearer picture of where the risks are will enable the UK to respond quickly and find effective ways of mitigating risks both proactively and reactively using the international levers available, and develop an understanding of how to best support established supply chains owned by private companies.

#### **Recommendation 4.4**

Assessing the UK's vaccines supply chain capability and building a mechanism which monitors and quality assures the resilience of global supply chains.

### **Fill Finish Capability**

The UK has seen a decline in pharmaceutical manufacturing infrastructure over the past 20 years and lacks the infrastructure to fill and finish drug substance into vials at a sufficient scale. Fill/finish is the term used to refer to this final stage in manufacturing.

There is a limited presence of CDMO (Contract Development and Manufacture Organisations) with manufacturing capability for the UK to rely on in the event of another pandemic, and the manufacture of vaccines requires highly dedicated and controlled manufacturing capability which is expensive to build and maintain and has long lead times for construction.

Maintaining a sterile pharmaceutical facility in a state of readiness profile presents significant challenges – keeping a fully trained workforce occupied and maintaining validated and qualified equipment without constant demand is not a viable solution.

It is critical the UK maintains the ability to surge manufacturing capacity domestically across the production process, and particularly at the fill-finish stage of vaccine delivery – and institute mechanisms to keep such capacity functioning in peacetime. While VMIC has fill finish capability using glass vials, it is important to ensure the UK has capability to manufacture vaccines of other formats such as oral, transdermal and intranasal.

#### **Recommendation 4.5**

Explore potential arrangements with UK based sterile manufacture facilities (CDMOs or pharmaceutical companies), who could provide surge capacity to fill and finish vaccines.

#### **Develop UK strategy to secure Adjuvant supply**

The UK does not currently stockpile adjuvants, unlike the US and Canada. However, adjuvants form key component of several COVID19 pandemic vaccines, such as protein adjuvant vaccines and whole inactivated vaccines developed by Novavax, GSK/Sanofi and Valneva as well as non-pandemic paediatric and adult vaccines including Shingrix, Anthrax, DT, DTaP, DTaP-IPV, DTaP-HepB-IPV, DTaP-IPV/Hib, Hep A, Hep B, HIB, HPV, Japanese encephalitis, MenB, and Pneumococcal vaccines.

The UK does not have any proprietary access to the most promising new adjuvants and should develop a deliberate strategy to secure their supply and consider whether stockpiling is a suitable approach.

**Recommendation 4.6:** develop a strategy to secure the supply of adjuvants

## **5. Launch a Future Vaccines Fund**

A Future Vaccines Fund would provide competitive funding for testing and evaluating novel vaccine formulations. The fund would support research that could lead to vaccines with the desired properties. This fund could be managed by Innovate with rolling competitive calls for targeted innovative ideas for vaccines, or a dedicated public/private, or solely private sector fund. Alongside UK government, leading global vaccine firms may be willing to invest to rapidly solve some of the shared challenges ahead. Sovereign Wealth Funds may additionally provide such investment as an insurance against future economic shocks.

Those projects that are funded would get access to the experts and activities in the proposed Centre for Vaccine Formulation and Delivery, access to the Clinical Immunology network and Clinical trials network as part of the funding.

### **Recommendation 5**

Launch a Future Vaccines Fund within UKRI/funded by private sector to advance innovation and support the research of novel formulations and formats.

## **6. Increase International Engagement & Collaboration**

To continue to build on our global leadership and realise the potential of multilateral working, the UK should strengthen its relationship with international partners in scientific collaboration in both industry and academic, continue its work with COVAX and ensure the latest data and intelligence is being applied to its strategy.

### **Enhance International Scientific Collaboration**

The development of vaccines with preferential characteristics for mass manufacturing, delivery and widespread application are a universal good. The UK will benefit from a diversified global pool of vaccines which are cheap and easy to manufacture at scale (including at UK sites), require less training to apply with simple storage requirements, driving down costs across the end-to-end process.

This is a clear recommendation from the Prime Minister in his Five Point Plan to be better prepared for future pandemics. Information sharing not only facilitates better and more effective scientific development globally by ensuring scientists have access to the best information possible but allows governments, NGOs and industry to more effectively track the progress of research and prepare accordingly.

The UK should build on the domestic objective to support development of vaccines with improved characteristics namely, scalable for mass production, stable at room temp, administered without a needle etc by securing wider buy-in to the optimisation of vaccine characteristics. This targeted optimisation work could strengthen existing initiatives, like WHO advice on Preferred Product Characteristics.

Most innovation relies on investments into biotech companies supported by academic insights and inventions. So the UK and its international partners could coordinate and focus their R&D funding on vaccines towards candidates with preferential characteristics.

As discussed in Nature<sup>2</sup> as Chair of the G7 in 2021, the UK could advocate for building flexible vaccine facilities around the world which are financially sustainable, operated by a well-trained workforce with tech transfer capabilities focused on the right technologies (not limited to injectables), and which can be commandeered for pandemic use when needed. The UK could help define key criteria for licensing a pandemic vaccine, including relevant ethnic bridging studies, which can be rapidly adopted by national regulatory agencies around the world so as to accelerate approval. These criteria would define safety and efficacy standards, as well as potential immune correlates from controlled human challenge studies. The UK could encourage countries to strengthen their own emergency use or conditional authorisation legislation now to enable the rapid distribution of a pandemic vaccines before full authorisation is secured, recognising that maintaining public trust is essential. The UK could encourage the sharing of trial data, bio-banking and research information internationally. This would build on existing guidance, like the Wellcome Trust 'statement on data sharing in public health emergencies'.

### **Recommendation 6.1**

Use the G7 chairman role to coordinate R&D funding into improved vaccine formats, promote expansion of global manufacturing capability, establish effective long-term information sharing, and encourage streamlining of global regulatory processes.

## **Secure a permanent future for COVAX**

The COVAX Facility has the potential to be a mechanism for international vaccine procurement and distribution in the event of a future pandemic. With development, COVAX has the potential to become a permanent fixture within the international health infrastructure.

The rationale behind establishing COVAX as a permanent mechanism for future pandemics is reflected in the current reasons behind the UK's commitment to COVAX as part of the solution to the COVID-19 pandemic. To defeat potential future global pandemics, we must work together to develop safe, effective, and affordable vaccines that can be produced quickly and made available to the world. COVAX has the potential to pool global resources and demand, expedite vaccine development and manufacture and tackle the challenge of equitable access. COVAX expands the UK's bilateral deals by providing access to a greater portfolio of COVID-19 Vaccines, this has the potential to be replicated in the event of a future pandemic. COVAX also ensures equitable distribution of vaccines to low-income countries.

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<sup>2</sup> Plan now to speed vaccine supply for future pandemics; <https://www.nature.com/articles/d41586-020-02798-0>

Currently it is unclear how a permanent COVAX would run. Concerns include:

- Whether a permanent COVAX would need longstanding members, and whether its membership could flux dependant on the circumstances of the pandemic at the time.
- How funding would work for COVAX if it was to develop into a permanent organisation.
- Whether the Office of COVAX would be disbanded post-COVID-19 pandemic, and how setting up these functions in the event of a future pandemic would work.
- Where and how the decision would be made to re-establish COVAX functions in the event of future pandemics.

### **Recommendation 6.2**

Establish COVAX as an international multilateral organisation for future pandemic preparedness.

### **Improve scientific literacy and industry knowledge within government**

To be an effective leader in the advanced manufacturing and vaccine development space, the UK government itself and its officials need to increase their level of scientific literacy and expertise. The work of the VTF has faced challenges in its work with staff who have little industrial expertise or scientific knowledge. Improving the scientific capability and experience in the government will increase the UK's international credibility and improve the success of global collaboration.

**Recommendation 6.3:** Increase the proportion of STEM graduates in the civil service to 50%; develop closer ongoing industry links to improve industrial understanding.