Written Evidence Submitted by the UCL Institute of Healthcare Engineering (C190105)

1. Background

The UCL Institute of Healthcare Engineering (IHE) is based at University College London. It brings together leading researchers working on the development of digital and medical technologies across five research themes – Prevention, Monitoring, Diagnostics, Therapies and Interventions, Rehabilitative and Assistive Technologies.

IHE is an interdisciplinary community with input from fields as diverse as engineering, health, human sciences, data and computing. These collaborations help to push the boundaries of thinking, encouraging fresh perspectives and the application of technologies to novel areas.

Its work is driven by the world's most pressing healthcare challenges and focused on delivering impact by creating solutions for real problems. This is only possible by the partnerships established over the years between clinicians, industry partners, patients and public.

This submission is a supplement to the UCL-wide inquiry response. It aims to provide more detail on the successful fast-track of innovation that resulted in the production of the UCL-Ventura CPAP device in record time.

2. Introduction

The UCL-Ventura project resulted from the needs raised by the Government[1] and the NHS in the context of the Covid-19 pandemic.

A consortium spanning UCLH clinicians, UCL engineers and Mercedes AMG High Performance Powertrains focused their combined expertise on large-scale manufacture of non-invasive respiratory support technology: continuous positive airway pressure (CPAP) devices.

CPAP had been used extensively in hospitals in Italy and China to treat Covid-19 patients. Intensive care unit capacity in both countries was quickly overwhelmed when mechanically ventilating patients needing more than facemask oxygen. CPAP provided a valuable bridge by providing non-invasive breathing support and has prevented around 50-60% of these patients from progressing to needing mechanical ventilation.

The UCL-Ventura CPAPs were manufactured at scale and so far, have been delivered to over 60 hospitals to treat Covid-19 patients, spanning England, the devolved nations, crown dependencies and overseas territories.

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[1] GOV.UK, "PM call with UK's leading manufacturers," ed, 2020. https://www.gov.uk/government/news/pm-call-with-uks-leading-manufacturers-16-march-2020

The design and manufacturing specifications for the UCL-Ventura CPAP device were made available at zero cost for humanitarian purposes to support the international community in building respiratory support capacity for Covid-19 patients. Within a month the blueprints had been downloaded by more than 1800 teams across over 105 countries spanning Europe, Asia, Africa, Americas and Australasia. Numerous countries are now developing their own prototypes, including Mexico, Peru, Cuba, Paraguay, Kenya, Bulgaria, Canada, the Philippines, India and Pakistan. UCL-Ventura devices have also been supplied directly via NGOs and philanthrophy to countries including Uganda, Palestine and South Africa

This project highlighted some of the key features needed to succeed in medical device innovation in response to an emergency outbreak as the Covid-19 pandemic.

3. The capacity and capability of the UK research base in providing a response to the outbreak, in terms of:

- ***advice to government, public bodies and others on managing the outbreak;***

After discussions with colleagues in Italy and China, UCLH intensivists realised that the UK needed more CPAP devices in hospitals to avoid ventilating Covid-19 patients where possible, and to preserve valuable healthcare resources. The UCL and UCLH team engaged in discussing this with the NHS and Department of Health and Social Care, , alongside the National Emergency Committee for Critical Care, and the NHS Guidance for treatment of Covid-19 patients was amended to include CPAP at the end of March 2020.

- ***the development and testing of therapeutics;***

The rapid mobilisation of an interdisciplinary team to focus on a clearly defined, immediate need was crucial, and was possible because of the long-standing collaborations between the academic, clinical and industrial partners. Just 100 hours after the first meeting, the first prototype was made and was being tested in a hospital on healthy volunteers. Crucially, CPAPs and associated kit (e.g. oxygen analysers) were not manufactured in the UK, and a partnership spanning clinicians, engineers and manufacturers enabled new devices to be designed and manufactured at pace, to meet the needs of COVID-19 patients in the UK.

4. The flexibility and agility of institutions and processes to respond on the above during a crisis including:

- **the availability and responsiveness of funding;**

The availability of funding straight from the start of the project was crucial for the quick deployment of the idea. However, most of the initial funding was provided by the project partners themselves.

[3] J. R. Greenland, M. D. Michelow, L. Wang, and M. J. London, "COVID-19 Infection: Implications for Perioperative and Critical Care Physicians," *Anesthesiology: The Journal of the American Society of Anesthesiologists,* vol. 132, no. 6, pp. 1346-1361, 2020, doi: 10.1097/aln.0000000000003303.

The UCL-Ventura team was backed up by the UCL Faculty of Engineering Sciences, who provided up front funding for testing and development. Having a significant amount of money unlocked at early stages meant the team could proceed with no financial constraints. The UCL Professional Services team also focused on supporting the programme, providing regulatory, communications, documentation and media support.

The partner company Mercedes HPP also contributed to the initial funding of the project. Their team effectively funded the development, and the repurposing of the manufacturing facilities in the short-term.

- Ultimately the UCL-Ventura team received an order of value £20M for 10,000 devices from the Department of Health and Social Care, which covered costs for development and mass manufacture.**the optimal functioning of regulatory and ethical processes;**

It took only 10 days from the first team meeting to achieving regulatory approval. The MHRA approved the UCL-Ventura CPAP device within only 36 hours of the application being submitted. This was only possible due to a close collaboration between the team and the regulatory body, which stayed in daily communication to facilitate the approvals process.

The team purposely focused on reverse-engineering an off-patent device, that has been used in the NHS for decades, because demonstrating like-for-like in terms of performance would facilitate the MHRA approval, and also there was a large body of clinical evidence for the safety and efficacy of the device. Mark II of the device involved design modifications to minimise oxygen utilisation and improve patient comfort, was approved by the MHRA days after the Mark I, and subsequently went forward for mass manufacture. The UCL-Ventura CPAP is a non-CE marked device, given approval for use in the NHS for the interest of public health protection under the Covid-19 pandemic emergency.

5. The capacity to manufacture and distribute testing, diagnostics, therapeutics and vaccines:

- **both standing capacity and capacity able to be mobilised;**

The UCL Institute of Healthcare Engineering connects engineers with clinicians, which enabled a common understanding of the unmet clinical need, and opportunity for continuous iteration and testing of the technology in hospitals.

The strong, pre-existing links between UCL Mechanical Engineering and Mercedes-AMG HPP provided unprecedented manufacturing capability, whilst maintaining high precision and an ability to respond at pace. The CPAP devices were produced at a maximum rate of up to 1,200 a day at the HPP technology centre in Brixworth (Northamptonshire) where the entire facility was repurposed to meet the demand.

Within one month of the start of the programme, the Department of Health and Social Care received the 10,000 UCL-Ventura devices that had been ordered. To-date, UCL-Ventura CPAP devices have been distributed to over 60 hospitals, working with logistics company G-TEM and their army of volunteers, who have expertly coordinated next-day delivery of devices and resupply of breathing circuits to hospitals across England, the devolved nations, crown dependencies and overseas territories.

6. The capturing during the crisis of data of the quantity and quality needed to inform:

- **decisions made during the crisis**

One of the UCL –Ventura team members was part of a network of intensivists that proved crucial to sharing data from the experiences of other countries in tackling the pandemic. Clinicians from Italy and China were in touch on a regular basis with UCLH clinicians to share lessons learned and provide information on changes in the care pathway for Covid-19 patients.

At the beginning of the pandemic, CPAP was not included in the UK clinical care pathway to treat Covid-19 patients, primarily because of concerns around spreading COVID-19 via aerosolization (discussed further in point 5), and the role that CPAP could play for COVID-19 patients. However, based on the evidence presented by clinicians in Italy and China (countries where the pandemic peaked earlier and so more experienced in treating Covid-19 patients), as well as mounting experience in the UK, these doubts were alleviated. This led to a change in the care pathway, on the 28th of March, with the addition of CPAP.

The UCL-Ventura team produced a suite of training materials (user guides, clinical instructions, training videos) and made data on the designs, and healthy volunteer evaluations available on a dedicated website. These enabled rapid and transparent communication and dissemination with intensive care and respiratory teams across the UK, and facilitated uptake of the Ventura CPAPs in NHS hospitals.

- **to maximise the learnings afterwards;**

Data on CPAP performance is being collected all over the World. In the UK, initial findings show that approximately 50% of patients treated with CPAP do not progress to mechanical ventilation, which is consistent with data from Italy.

The clinical protocol for the use of CPAP has evolved, and so has the UCL-Ventura CPAP itself. This resulted in direct upgrades to the device, and resubmissions to the MHRA. The team has been continuously sharing the lessons learned with other manufacturers and clinicians around the world, via a programme of webinars, and through their dedicated website

Medical oxygen is a limited resource and to cope with demand, not only in the UK but also in resource limited settings, in particular Low and Middle-Income Countries. Continuous characterisation studies on the flow and pressure need to operate CPAP devices effectively are happening to maximise oxygen utilization and future response.

The UCL-Ventura team is also working on numerous publications with important data to communicate in advance of subsequent waves.

7. The mechanisms for communication of scientific evidence internationally, within national governments and with the public:

- **including the handling of conflicting scientific opinions;**

Transmission of the coronavirus from patients to healthcare workers is a cause of concern. It has been debated whether use of pressurised oxygen, as CPAP devices require, can generate aerosolization, thereby exposing healthcare workers to the virus[2].

To handle the conflicting opinions on the risk of aerosolization, the UCL-Ventura team collated data on healthcare workers infections both nationally and internationally, and also supported environment testing on CPAP wards at UCL.

These studies returned no evidence of Covid-19 in air samples as close as 1 metre from CPAP patients (unpublished). This experimental data, together with the widespread use of CPAP in many countries, and the fact that infection rates have not increased in healthcare workers looking after such patients[2,3] were presented as evidence to support the use of CPAP. In fact, only around 8% of healthcare workers in critical care at UCLH have COVID-19 antibodies, compared to 15% in the general population.

There were also significant concerns around the oxygen utilisation of CPAPs, given the unprecedented demand on medical oxygen in hospitals. CPAPs are typically viewed as 'oxygen hungry' compared to mechanical ventilators. The team modified the Mark I device design (e.g. the air entrainment port, and patient circuit configuration), reducing oxygen utilisation by up to 70%, and also tested the impact of using many CPAP devices in the same ward on the ward oxygen supply. Nonetheless, given the importance of the issue and variability in individual hospital oxygen supplies, all Ventura devices came with clear messaging around the importance of working with local oxygen engineers to plan how to use a hospital's oxygen delivery capacity. All data on oxygen utilisation were also made available on the Ventura website.

On a final note, it was only possible to deliver vital healthcare technology to the NHS frontline because of the pre-existing relationships across the university, hospitals and industry.

(August 2020)

[2] N. Arulkumaran, D. Brealey, D. Howell, and M. Singer, "Use of non-invasive ventilation for patients with COVID-19: a cause for concern?," (in eng), *Lancet Respir Med,* vol. 8, no. 6, pp. e45-e45, 2020, doi: 10.1016/S2213-2600(20)30181-8.

[3] J. R. Greenland, M. D. Michelow, L. Wang, and M. J. London, "COVID-19 Infection: Implications for Perioperative and Critical Care Physicians," *Anesthesiology: The Journal of the American Society of Anesthesiologists,* vol. 132, no. 6, pp. 1346-1361, 2020, doi: 10.1097/aln.0000000000003303.