BACKGROUND PAPER

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High Level Panel Discussion on Innovation and Investing in medical Devices and PPEs

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During the COVID-19 pandemic there have been worldwide shortages of critical personal protective equipment (PPE) and medical devices, primarily ventilators and oxygen therapy devices. In response to the increased demand for these technologies during the pandemic, the U.S FDA enacted Emergency Use Authorizations (EUA) during the COVID-19 crisis[1] to expand the availability of PPE, ventilators, and other critical medical equipment. EUAs intend to increase the availability of PPEs and medical devices to respond to the COVID-19 crisis by allowing flexibility for manufacturers to make appropriate modifications to the design of these devices to address current supply shortages. These special authorizations have led to the development of innovative design and manufacturing approaches for PPE and ventilator technologies. Although the increased need for these technologies has sparked the development of open source and locally and rapidly manufactured solutions, there are many design and manufacturing standards that must be followed to uphold quality.

1 PPE

Personal protective equipment (PPE) has been proven to reduce the spread of the COVID-19 virus. Common types of PPE include masks, respirators, face shields, protective goggles, gowns, aprons, and gloves. Although PPE demand is increasing, quality cannot be sacrificed. Several national and international organizations have published guidelines on the design, manufacture, use, and re-use of PPE for both medical and community settings. WHO and ASTM have curated standards and regulations pertaining to the design of different kinds of PPE on their websites.[2,3] International and national organizations, such as WHO,[4] the U.S CDC,[5] and the African CDC[6] have published guidelines on the selection and appropriate use of PPE in the context of the COVID-19 pandemic, which emphasizes factors such as sterile/non-sterile use, material types, durability, and type of exposure expected, among others. Several online community groups focused on developing open-source PPE designs have also surfaced, such as the *Open Source COVID-19 Medical Supplies* Facebook Group, which, as of June 2020, has over 70,000 members from around the world,[7] and working groups organized by Mass General Brigham.[8] The UK government has published guidelines[9] to speed up adoption of these open source designs that may be lacking CE certification. Finally, regional occupational health and safety guidelines may also be used as guidance for the selection and use of PPE for different scenarios, including the appropriate selection of a face mask and gloves for different environments.

1.1 Medical/Surgical Masks

Face masks have proven to be an important tool for the general public in the prevention of the spread of COVID-19. There are two standards specific to face masks: BSI 14683:2014,[10] which discusses specifications for construction, design, performance requirements, and test methods for face masks, and ASTM F2100,[11] which discusses classifications, performance requirements, and test methods for materials used in the construction of face masks. Due to the shortage of face masks worldwide, the U.S CDC has released guidelines on the manufacturing, wearing, and washing of cloth face masks[12] and the WHO has released guidelines on the use of masks in communities, home care, and health care settings.[13] And, most recently, the WHO specified that cloth masks must include at least three levels of different material layers in.[14]

1.2 Respirators

Respirators have higher particle filtering capabilities when compared with medical/surgical masks, and the N95 masks are considered the 'gold standard' (N95 masks are defined by masks that filter at least 95% of 0.3um airborne particles). There are two standards that pertain to respirators: BSI 14683:2014,[15] and EN 149:2001+A1:2009,[16] which is a European standard on the minimum requirements for filtering face masks and includes a list of performance tests to assess the compliance of masks with filtering requirements. There exists tests and standards for air-purifying particulate respirators, including a set of tests for determining respirator filtering capabilities.[17] The U.S CDC has also released guidelines pertaining to methods of decontaminating respirators,[18] extending the use of N95 masks,[19] and a list of NIOSH-approved particulate-filtering respirators.

1.3 Face Shields

Face shields are a recommended form of PPE for healthcare workers involved in direct care of COVID-19 patients.[20] However, despite the wide use of face shields in the medical community, there are few standards and guidelines specific to their design. Two standards pertaining to face shields are EN 116, "Personal Eye Protection standards" from the EU[21] and ANSI Z87.1-2020 Standard.[22] During the COVID-19 crisis, various groups have stepped up to construct face shields in response to the need from healthcare providers. To this end, some groups, including *Coronavirus Makers*, have guides for assembling face shields on their open source website, which makers can use to construct shields.[23] The U.S FDA issued guidelines for face shield construction during the pandemic to ensure that protective equipment meant for health care workers would provide sufficient protection.[24]

1.4 Protective Goggles

Due to the possibility of the COVID-19 virus entering the human body through eyes, protective goggles are recommended as a form of protection. Face shields have shown to be more popular than protective goggles in fighting the pandemic and so there are no published COVID-19 specific guidelines from national and international organizations regarding their use. There are three standards relevant to goggle design: EN 116, "Personal Eye Protection standards" from the EU,[25] ANSI Z87.1-2020 Standard,[26] and AS/NZS 1337.1.[27]

1.5 Surgical/Medical Gowns

Gowns are primarily worn by workers in the medical field who can come in direct contact with COVID-19 patients. There are two standards specific to medical gowns: a standard published by the U.S FDA[28] and ANSI/AAMI PB70 - Class 3, which outline requirements for design and testing of gowns used in different risk environments.[29] The UK government published guidelines[30] for potential manufacturers interested in donating supplies for frontline health care purposes. The U.S CDC published guidelines[31] for strategies in optimizing the supply of isolation gowns targeted primarily at policy makers.

1.6 Aprons

In addition to gowns, aprons are also being increasingly used for protection by healthcare workers. There are three specific standards pertaining to aprons and other protective clothing. ISO 13688:2013 specifies general performance requirements for ergonomics, innocuousness, size designation, ageing, compatibility and marking of protective clothing, and is to be used in conjunction with other standards (i.e., it is not a standalone standard).[32] There are two European standards: EN 14126:2003,[33] which outlines requirements and test methods for reusable and limited-use clothing for the protection against infective agents, and EN 13795:2011+A1:2013,[34] which focuses on the manufacturing and processing requirements of protective clothing for use in medical care environments. There are limited COVID-19 specific guidelines about the use of aprons.

1.7 Gloves

Gloves are primarily used by medical care workers but have become more prevalent in public settings such as in markets, restaurants, and other small businesses. There are two overarching standards for gloves: ANSI/ISEA 105-2016, which addresses the classification and testing of hand protection,[35] and ASTM D6319 - 19, which outlines test procedures for evaluating performance and safety of nitrile examination gloves.[36] Further, the U.S CDC provides guidelines for optimizing the supply of disposable medical gloves.[37]

2 Medical Devices: Ventilators

Medical oxygen has become a primary treatment for severely ill and critical COVID-19 patients. To provide this treatment, oxygen therapy devices are needed for oxygen distribution, oxygen regulation and conditioning, and oxygen delivery and patient monitoring. In any context, the use of these devices will heavily depend on both the availability and quality of care, including the availability of trained professionals for operation and maintenance. To ensure safety and effective use of oxygen therapy devices in the context of COVID-19, medical personnel must be trained to select and operate equipment for the treatment of severely ill and critical patients suffering from Severe Acute Respiratory Infection (SARI). WHO has created an interim guidance for the clinical management of COVID-19.[38] Medical online knowledge platforms such as MedCram[39] and many institutions including Harvard University[40] and the American Heart Association CPR & First Aid[41] have also published crash courses on oxygenation and ventilation of COVID-19 patients.

For the management of COVID-19 patients, priority oxygen therapy devices suggested by WHO[42] include oxygen concentrators and medical gas cylinders for oxygen distribution; flowmeter, invasive and non-invasive ventilators for oxygen regulation and conditioning; nasal cannula, masks, tubing, nasal catheter and high-flow nasal cannula for oxygen delivery; and pulse oximeters for patient monitoring.

To treat COVID-19 patients at the primary level of the health system, Basic Oxygen Therapy equipment needs to be procured. The WHO-UNICEF technical specifications and guidance for oxygen therapy devices details product specification[43] for a wide range of products for delivering basic oxygen therapy and provides guidance on their selection, procurement, use and maintenance. In the context of COVID-19, this equipment includes oxygen concentrators/and or oxygen gas cylinders, flowmeters, bubble humidifiers, nasal cannulas/masks/tubing and finger-tip pulse oximeters. Flowmeters are required as a separate device only when using oxygen gas cylinders as the source since oxygen-concentrators have built-in flowmeters. Pulse oximeters need to be prioritized in primary and secondary level health care facilities. During intensive or emergency care settings, these devices can provide constant monitoring of the patient's oxygen saturation levels which are necessary for healthcare workers to identify when a patient needs oxygen therapy and measure the ongoing success of the therapy.

At the secondary and tertiary levels of the health system, invasive critical care ventilators and non-invasive ventilators, mainly continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) and high-flow oxygen systems, have been recommended as essential equipment to treat COVID-19 patients. WHO created an interim guidance of the technical specifications for invasive and non-invasive ventilators for COVID-19.[44] This document includes the minimum requirements these devices must comply with and important procurement considerations such as trained personnel and infrastructure requirements for safe use. Most notably, invasive ventilators require well-trained medical staff to perform the intubation and to manage the pressure setting controls and alarms whereas non-invasive ventilators avoid intubation and are easier to use once the right interface is applied. Additionally, invasive ventilators should only be used in settings with high-pressure oxygen or air sources, controlled temperature and humidity, and technical staff to perform troubleshooting protocols, maintain the equipment and for decontamination procedures.

Shortages of ventilators worldwide and their high prices in conjunction with the widespread use of digital modeling and manufacturing technologies, have made governments resort to locally and rapidly manufactured ventilators. AAMI has recently published end user disclosures and design guidance for Emergency Use Ventilators (EUV), Emergency Use Resuscitator Systems and CPAP/BiPAP devices[45] MHRA from the UK government has issued specifications of the minimally clinically acceptable Rapidly Manufactured Ventilator Systems (RMVS)[46] and Rapidly Manufactured CPAP Systems (RMCPAPS)[47] to be used in UK hospitals during COVID-19 pandemic. The ASA-APSF has recently published guidelines on the use, set-up, monitoring and maintenance of anesthesia ventilators safely as ICU ventilators for COVID-19 patients.[48] Additionally, the ASA-APSF issued a joint statement with the SCCM, AARC, ASA-ASPF, AACN, and CHEST about placing multiple patients with respiratory failure on a single ventilator in the context of COVID-19;[49] advising not to attempt to ventilate multiple patients with a single ventilator since it can increase the mortality rates and recommending to purpose each ventilator to the patients that are most likely to benefit from the treatment.

The need for rapidly manufactured and high-quality medical grade equipment has brought together a global community of engineers, manufacturers, physicians, regulators and others. Several online community groups focused on developing open-source ventilator designs have surfaced such as Open Source Ventilator (OSV)[50] Ireland and OpenLung Canada.[51] Global innovation challenges have been launched such as the Code Life Ventilator Challenge[52] by the Montreal General Hospital Foundation in collaboration with the Research Institute of the McGill University Health Centre (MUHC) which aims to select low-cost ventilator designs based on previously established technical requirements,[53] medical device compliance requirements,[54] and material guidelines.[55] Diverse open-source emergency use ventilator projects have been

started such as MIT's Emergency Ventilator (E-Vent) Project,[56] which also lists key specifications and experimental protocols for use by the greater online maker community. Companies such as Medtronic[57] have posted design specifications for their Puritan Bennet 560 (PB560) ventilator which can be used by makers under a permissive license.[58] Any design developed by engineers, makers, or small medical device companies should comply with medical device regulations on electrical safety, clinical efficacy, electromagnetic compatibility, biocompatibility, risk mitigation and sterilization. Materials used for fabrication should be suitable for biocompatibility of respiratory device standards. Additionally, developers must refer to standards for material selection of parts that could be exposed to heat. The U.S FDA provides guidance on technical considerations for additive manufactured medical devices.[59] National health regulating authorities should distribute explicit certification requirements for the design and manufacturing of ventilators; authorities need to make sure the developers of these technologies have a clear understanding of the test protocols approved by the regulating entity.

3 Manufacturing Innovations for Medical Devices and PPE

There are clear guidelines on the best practices for the design of PPE and medical devices, but one of the main barriers to distributing PPE and ventilator technologies to individuals around the world is a manufacturing bottleneck, meaning current manufacturing capacity cannot keep up with demand. As such, several manufacturing innovations have sprouted since the beginning of the COVID-19 pandemic. Many large companies, such as Tesla, Ford and GE, and GM, have committed to use their factories for PPE, ventilator, and oxygen therapy device production.[60] Government initiatives such as the UK's Ventilator Challenge[61] have contributed to supply the demand for ventilators by creating a consortium of industrial, technology, and engineering businesses from the aerospace, automotive and medical sectors. As a result of this initiative, engineering businesses such as Airbus and Smiths Medical have partnered to manufacture existing ventilator designs. Several African clothing manufacturers have adopted their facilities with the help of international organizations such as the International Finance Corporation to produce PPE.[62] Repurposing existing manufacturing facilities requires, at the minimum, reconfiguration of manufacturing floor layouts and, at the other end, the purchase of new equipment and certification from regulating bodies if specialized equipment, such as N95 masks and ventilators, are to be produced. Since these processes take time, learning best practices for factory reconfiguration is an on-going learning process. Several organizations, such as Next Generation Manufacturing Canada[63], have launched initiatives, with an open call to the public, to fund companies interested in modifying their facilities for the manufacturing of PPE, ventilators, and oxygen therapy devices.

The use of 3D-printing for manufacturing PPE and high-end medical equipment has also risen in popularity and has proven to be an effective decentralized manufacturing method.[64] To appropriately adequate digital fabrication facilities, further development on Quality Systems (QS) requirements is needed for medical equipment manufactured through 3D printing technologies. If 3D printing technologies are used, it must be taken into consideration that 3D printing creates intrinsic porosities and additional techniques might be required to seal surfaces and limit leaching of components. Protocols must be established around adequate cleaning, sterility and biocompatibility of 3D printed medical devices. The U.S FDA provides guidance on QS requirements for regulated medical devices made in whole or in part by 3D printing methods.[65] National health regulating authorities should require that these emerging facilities seek compliance with Quality Management Systems (QMS) standards for medical device manufacturers such as the ISO13485.

There is a need for regulations and manufacturing protocols for medical products that can be produced through modern digital fabrication methods in case a global crisis hinders supply of the required equipment. Currently makers and small medical device manufacturers that have not been able to reach co-operation agreements with traditional medical device manufacturers to ramp up production of these devices and had opted to apply reverse-engineering or design from scratch, have been slowed because of Intellectual Property protection and high medical standards requirements. A living database of peer-reviewed medical grade products coupled with a network of ISO13485 manufacturing facilities, could speed up the process of research and development and would allow rapid manufacturing of the needed devices. The U.S NIH's 3D Print Exchange platform intended to share scientifically accurate or medically applicable models, developed a COVID-19 supply chain response initiative that includes models for nasal and throat swabs for sample collection, face shields and mask.[66] Blockchain technology could potentially be considered as a tool to enable secure storage and exchange of digital products such as components of medical devices required in an emergency setting like the COVID-19 pandemic. [67]

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