Innovation Amid a Pandemic: How Low-Cost, High-Quality Ventilators Became a Reality

Neil P. Ray, MD

Much has evolved since the early days of the COVID-19 pandemic, but I am sure the events of spring 2020 are still fresh in all our minds. Reports in early 2020 shared that the SARS-CoV-2 virus had migrated from Wuhan, China, and shortages of critical care resources in Italy and Spain were costing lives. Just as the COVID-19 pandemic began its spread in the United States and took its first lives here, President Trump revealed that the U.S. might be short more than 130,000 ventilators in preparation for the COVID-19 pandemic. After reading a New York Times article on March 18, 2020, "There are Not Enough Ventilators to Cope with the Coronavirus," I, along with many of my anesthesiology colleagues, wondered if our MacGyver instincts that we use to fix broken OR equipment might be applied to the anticipated ventilator shortage.

As a board-certified anesthesiologist and the CEO and founder of a medical device company, sitting in the middle of the medtech ecosystem in Silicon Valley, I kept asking myself what we could do about the potential ventilator shortage.

Designers used the BVM bag in a novel fashion and developed a piston design to deliver positive pressure. This preserves the BVM bag from being squeezed too many times and allows for more precise ventilator settings to be utilized.

Neil P. Ray, MD
Founder and CEO, Raydiant Oximetry, Inc., San Ramon, California.

From idea to reality

I discussed the potential ventilator shortfall with Russ DeLonzor, the COO and President of Raydiant Oximetry, the company I founded. Russ, an experienced medical device executive in R&D and operations, got his start in the industry with 12 years at Nellcor Puritan-Bennet (and its successors). So, in addition to his pulse oximetry expertise, Russ has a strong background in ventilator mechanics and a very deep network of associates in the ventilator business. We agreed we had to do something.

Within a few days, we organized a call with a few other key medical device leaders and agreed to found Respirana, Inc. with the mission of developing an ultra-low-cost simple ventilator. We then quickly recruited a cross-functional group of over 30 medical device experts to join the effort, including engineers (software, industrial design, electrical, and mechanical), quality and regulatory, operations, marketing and finance personnel, and, importantly, physicians and others with clinical perspective.

Even if we could design and build a ventilator for rapid deployment, how would we get it through the FDA approval process? The usual pathway to clearance could be costly and time-consuming. On March 24, the U.S. Department of Health and Human Services secretary authorized the emergency use of ventilators, and the Association for the Advancement of Medical Instrumentation subsequently published design guidelines for device manufacturers seeking Emergency Use Authorization. These outlined exactly what standards and validations a medical device would need for Emergency Use Authorization for a novel ventilator. The simple devices we were working on would fall into the FDA's most basic, newly outlined class of ventilator, Emergency Use Resuscitation Systems. The provision of these guidelines established an important difference for our effort, compared with more typical medical device startups. We would not invest customary time researching the market and customer needs. We had a navigable roadmap.

> **"We have developed a clearer vision for our product roadmap through three distinct product offerings, which will be critical in realizing our vision to one day offer a full-functioning critical care ventilator to developing countries for under $1,000."**

Early days

Initially I served as the medical advisor and developed the minimal viable specifications the ventilator needed to treat COVID-19 patients with acute respiratory distress syndrome (ARDS). Leaning on my network of anesthesiologists familiar with medical device development (Steven L. Shafer, MD, Editor-in-Chief, *ASA Monitor*; Ted McKean, MD, MBA, Angel MD network; Chris Apfel, MD, Keiretsu Forum, and Gary Goldman, DDS, MD, Global Health Impact Fund), we examined optimal setting ranges for the type of device we had in mind, including tidal volumes, respiratory rates, I:E ratios, and maximum pressure suitable for treating COVID-19 patients with ARDS. The guidelines provided direction on these settings, but we wanted to get the right balance of trade-offs in clinical relevance, reliability, and simplicity (manufacturability/cost) in setting our specifications.

Under the threat of a rapidly spreading global pandemic, we needed to prioritize speed to production, production source-ability, cost, and scalability. We knew that the existing ventilator manufacturers increased production of conventional ventilators, but we knew that increasing production would be slow because of supply chain and production constraints.

As we ramped up our efforts, several academic groups, engineering teams, and unrelated businesses (Virgin Orbit, Fitbit, etc) were developing automated Bag-Valve-Mask ("BVM", aka, "Ambu bag") compression devices. These initiatives garnered considerable attention in the press. These forms of Emergency Use Resuscitation Systems were what the FDA had in mind when the category was created. In fact, we developed our own design and prototype of such a "bag-squeezer" and still believe it to be one of the best in terms of mechanical design. However, we were concerned that a BVM approach might have reliability issues if used for days or weeks in critically-ill ARDS patients. Ambu-bags were not really designed with high cycle counts of mechanical actuation in mind. Our ideal design, therefore, would be more robust than an automated "bag-squeezer" but still meet our other design objectives and be suitable for the relevant challenging care settings we anticipated.

During the first week in April, our team of engineers had their "Eureka!" moment for the design. Building off similar piston-driven designs from the past, we decided to use the BVM bag in a novel fashion and developed a design with a very basic piston motor to deliver positive pressure. The BVM bag, used only as a reservoir, is not under duress and delivery of breaths can be more precise, while keeping costs low and scalability intact. While the entire team sheltered in place, we assembled a proof-of-concept device and filed three patent applications, including one specifically for this innovative design.

By the third week of April, the team had iterated on several prototypes and the time came to validate our design and performance expectations the FDA had outlined. Several of my fellow anesthesiologists made valuable contributions during this stage. Jim Philip, MD, MS, from Brigham & Women's Hospital, Boston, and Ted McKean, both helped arrange for us to borrow critical test equipment such as flow meters and test lungs.

Strategy and execution

While designs were researched and developed, the founding leadership team was having internal discussions about the long-term goals for the project. There were many "open source" and philanthropic efforts taking place to address the feared ventilator shortage, but we believed the most pragmatic course to be as a commercial enterprise, working with existing companies along the medical device supply and distribution chain. We also felt the unmet need around the world for a low-cost, high-quality ventilator would persist beyond the COVID-19 pandemic and wanted to position our endeavor for long-term viability. Hence, a corporation was formed with a legal structure of a Delaware C-Corporation. We named the corporation Respirana, which means "to breathe again." Next, we established a board of directors, appointed cofounder Tom Hillman as our acting CEO and CFO, and began developing initial product names, a company logo, and similar collateral.

We successfully completed our validation studies and submitted our Emergency Use Authorization request to the FDA on April 24, 2020. It was an incredible feat for our "volunteer army" to come together to design, develop, and validate a ventilator solution in just over a month.

Next steps

As we charged ahead through spring 2020, the pandemic and world around us, as well as our circumstances, rapidly changed. In May, we had iterated a few times with the FDA and addressed follow-up questions on our Emergency Use Authorization submission. We had made good progress in developing critical relationships and agreements with suppliers and contract manufacturing candidates for our first-generation device. We capitalized through the development of a working prototype and Emergency Use Authorization submission, with a plan for full capitalization once authorization was granted.

But circumstances continued to evolve around us in important ways. An unprecedented effort to stop the pandemic's spread with sheltering-in-place, social-distancing, and wide-scale use of masks helped control the spread. Scientists and doctors made important strides in improving therapies and outcomes in treatment of serious COVID-19 patients. Both positive trends significantly helped reduce the need for critical care ventilators. Simultaneously, the world's existing ventilator manufacturers had dramatically stepped up production, bolstered by billions of dollars in contracts with the HHS, for essentially 10 years' worth of production. By mid-May, it was becoming clear that there would be no global shortage of ventilators in 2020 due to COVID-19. Through this period, Dr. Shafer helped us understand both near- and longer-term domestic and global implications related to the pandemic. Coincidentally, the pace of FDA authorizations of new ventilators slowed to a trickle. Though we had addressed every question posed by the FDA and been told our submission appeared complete, we began to realize that the immediacy of this regulatory pathway might be in doubt.

Nevertheless, Respirana continued through the summer and into fall, making steady progress. We've continued to improve on our first-generation device and taken the opportunity to build out our team with more seasoned ventilator and respiratory care expertise, particularly on the clinical, marketing, and sales sides. This has enabled more thorough market research, strategy development, and product road-mapping that time did not allow for in the early days. We are now working with the FDA to map out our efforts to achieve 510(k) clearance for our first device. We have identified a compelling patient care use-case for our first-generation device, as a revolutionary hands-free automated resuscitator for use in ED, intra-hospital transport, and stretched ICU settings. By the end of 2020, we will have conducted clinical forums and focus groups to validate this value proposition, a great foundation for raising the next round of investment capital. Dr. McKean, now officially an advisor to Respirana, will be spearheading our investigation into military-specific use cases for our device. We have developed a clearer vision for our product roadmap through three distinct product offerings, which will be critical in realizing our vision to one day offer a full-functioning critical care ventilator to developing countries for under $1,000. Along the way, we continue to benefit from important clinical, innovation-oriented, and capital-related contributions from anesthesiologists. I'm proud that Respirana stands as another great example of the broadening impact of our profession. ■

Survey Results

Continued from page 1

Payment concerns

Payment and reimbursement issues can be difficult to navigate, but it is crucial anesthesiologists receive compensation that coincides with the value of the services they provide.

"This is an issue that can be difficult to explain to regulators and elected officials," said Sam Page, MD, FASA, Chair of ASA's Committee on Governmental Affairs and County Executive of St. Louis. "Anesthesiologists should be comfortable outlining their role in patient care and why it is important to be fairly compensated for the work that they do.

"Equitable compensation is crucial to ensure we can continue to provide our expertise and that anesthesia services are available to patients who need surgery," he continued. "Anesthesiologists must learn how to navigate the regulatory side of health care."

Resources are available to help anesthesiologists hone their skills for tasks outside the clinical setting. For example, anesthesiologists can join ASA Team 535 and contribute to efforts focused on building strong relationships with each member of Congress.

"This is a way to take a proactive approach when it comes to addressing regulatory issues, such as reimbursement," Dr. Page said. "Not only will you stay current on the latest issues before Congress, but you will also learn how to be most effective in your communication."

Catlin Nalley is a freelance medical writer based in Jacksonville, North Carolina.

Resources for the Anesthesiologist

Whether you are looking for ways to stay current on the latest regulations or advocate for the profession, here are a few helpful tools:

- ASA Team 535: Support the specialty by building relationships with members of Congress (**asamonitor.pub/3lGwgr2**).
- *ASA Monitor*: Stay informed on legislative and regulatory news (**asamonitor.pub/2QYIaP3**).
- ASA e-newsletters: The latest guidelines delivered straight to your inbox.
- Grassroots Network: Take action and engage with your elected officials (**asamonitor.pub/3i2d4l6**).
- ASA Advocacy Modules: Learn how to get involved in advocacy efforts (**asamonitor.pub/2YVkD5P**).

Regulatory Challenges in Anesthesia Practice

	Extremely concerned	Very concerned
Payment	25%	34%
The Joint Commission guidelines	14%	31%
Changing/conflicting regulations	12%	28%

The Joint Commission guidelines

TJC and its guidelines can be a challenge for any practice. However, this is not something that can be avoided and, therefore, must be addressed head on.

"Anesthesiologists must be familiar with the guidelines. Anyone who works in a hospital knows that The Joint Commission visits can be frustrating," advised Dr. Page. "It is important to work closely with your hospital leaders to make sure that you are up to date and understand what the expectations are, so that you can do the hard work to meet those expectations.

"On occasion, they may ask for something that does not seem reasonable," he noted. "The ASA has representatives on The Joint Commission. When you have concerns you should voice them, so these representatives can advocate for you and our profession."

Changing/conflicting regulations

Regulations change often and can sometimes conflict with one another, so it can be difficult to navigate them when making clinical decisions.

"Make the time to stay current on the latest updates," Dr. Page said. "The *ASA Monitor* and ASA e-newsletters are an efficient way to remain apprised of the latest regulations. I know that we all receive a lot of emails, but our commitment to keeping our patient safe requires us to stay current on any changes." ■