CASE STUDY: EMERGENCY USE AUTHORIZATION (EUA) OF A DECONTAMINATION SYSTEM FOR PERSONAL PROTECTIVE EQUIPMENT (PPE) DURING THE COVID-19 PUBLIC HEALTH EMERGENCY

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CLIENT
Sterilization Equipment Manufacturer

PRODUCT
Hospital Point-of-Use Decontamination System for PPE

REGULATORY PATHWAY
Eligible for an EUA for Medical Devices Related to COVID-19

SERVICES PROVIDED
Feasibility & Efficacy Testing
Project Planning & Management
Regulatory & Quality Support
Pre-EUA Preparation & Submission

CLIENT NEED

NovaSterilis Inc. is a US-based company that designs, develops, and manufactures sterilization equipment based on its novel supercritical carbon dioxide ($scCO_2$) technology platform. Over the last decade, the NovaSterilis platform, which is comprised of an instrument (Nova2200™), process-specific software, and a sterilization additive (NovaKill™), has been used in the tissue banking and regenerative medicine industries.

Based on their longstanding history working with medical products, NovaSterilis recognized in early in the COVID-19 pandemic that its platform was capable of meeting the technical needs of the healthcare industry and could provide seamless integration into the current workflow of hospitals not located in large metropolitan areas. Although NovaSterilis has been commercial for over a decade, they did not have an in-house regulatory team that could plan and file an FDA submission that was needed in a few weeks as opposed to several months. iFyber was contracted by NovaSterilis to 1) evaluate the viability of their $scCO_2$-based technology for single-user reprocessing of N95 respirators, 2) develop the FDA emergency use authorization (EUA) submission strategy and testing plan, 3) perform the required testing both independently and in conjunction with the NovaSterilis team, and 4) author and submit an EUA request for the distribution and use of the Nova2200 platform in the hospital setting.

Due to the time-sensitive nature of the emerging health crisis NovaSterilis required quick mobilization of resources and seamless integration with their existing team. The goal was to allow current NovaSterilis employees to maintain existing projects and provide support in their areas of expertise to embedded iFyber personnel. iFyber team members lead the FDA submission efforts through their regulatory experience and complimentary scientific knowledge. This strategy was cost-effective for NovaSterilis, but more importantly, it allowed them to go from idea to FDA submission in 24 days.

CHALLENGE

During a public health emergency, such as the COVID-19 pandemic, FDA can use EUA authority to allow the use of unapproved products to diagnose, prevent, or treat serious or life-threatening diseases when there is no adequate, approved, or available alternative. Only those medical products that may be effective to prevent these diseases can be considered as possible EUA products – FDA assesses potential effectiveness on a case-by-case basis using a risk-benefit analysis and available scientific evidence.

iFyber was tasked with supporting NovaSterilis throughout the EUA process, including building and executing the regulatory strategy and testing plan to support effectiveness claims and demonstrate a favorable risk-benefit ratio. The time frame between project initiation (i.e., initial proof-of-concept runs) and pre-EUA submission was required to be less than one month based on the fast-moving public health situation. Testing requirements included validation of bioburden reduction, material and respirator compatibility, evidence that the process did not pose any health hazards due to process residuals, and determination of the maximum number of decontamination cycles that do not affect respirator fit or function.

LIMITATIONS

There were several limitations that needed to be overcome during this effort. Due to supply shortages, N95 respirators available for testing were extremely limited and were being prioritized for use and reuse by healthcare personnel (HCP). As a result, it was particularly important to be judicious in our testing approach—all testing had to be meticulously planned and executed to ensure appropriate allocation of respirators to meet project goals without funneling away important resources for HCP. Further, with the increased demand for respirator-specific manufacturing and testing, it became increasing difficult to engage with external vendors due to large backlogs. Alternative strategies and creative solutions were required.

Lastly, the NovaSterilis platform is not FDA-cleared as a general use sterilizer and is classified as a novel sterilization methodology by the FDA. The FDA therefore requires extensive device characterization, thorough process descriptions, and a greater amount of supporting data to demonstrate that the technology is safe for users and efficacious. As compared to EUAs requested by other (larger) manufacturers with previously cleared medical devices (e.g., vaporized hydrogen peroxide) this translated into a more detailed submission package and increased review timelines. Following initial pre-EUA meetings, direct and consistent communication was maintained with the FDA review team. This allowed iFyber to make certain that all testing and resulting submissions appropriately and concisely

addressed both the guidance provided and any additional questions posed by the review team.

PROCESS

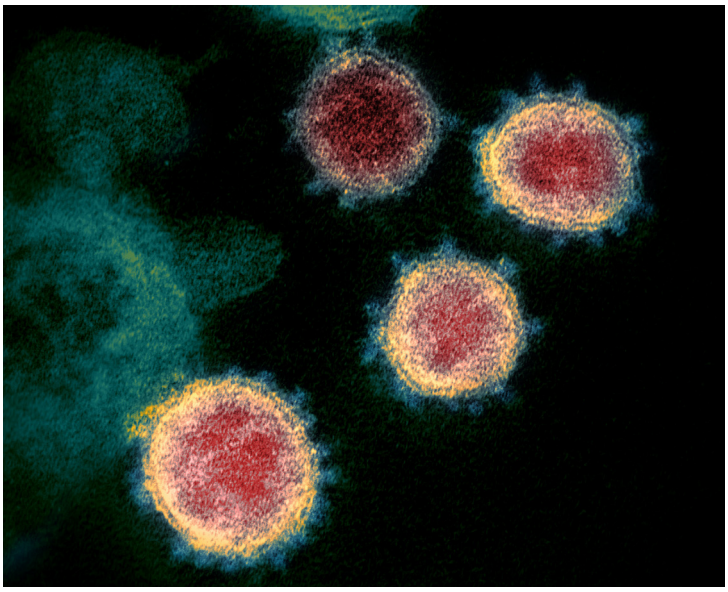
iFyber brought together a multi-disciplinary and highly experienced project team with expertise in microbiology, material science, chemistry, project management, quality systems, and regulatory strategy and submissions. Over the duration of the project, the iFyber and NovaSterilis teams met daily to review project objectives, testing progress, and discuss and troubleshoot challenges. A timeline of events is shown below.

REGULATORY STRATEGY AND TEST PLAN

While initial proof-of-concept runs were performed to ensure N95 respirators could withstand the NovaSterilis process and appropriate levels of microbial inactivation were reached, iFyber developed a detailed and targeted project plan based on applicable FDA guidance documents and discussions with the Agency. iFyber had previously provided regulatory consulting to NovaSterilis (e.g., Information Q-subs and Meetings) in support of an FDA Innovation Challenge Grant they were awarded for evaluating $scCO_2$ sterilization technology as an industrial alternative to ethylene oxide sterilization. During the initial phases of the EUA project, iFyber's regulatory lead reached out to these existing contacts within Surgical and Infection Control Devices (Office of Health Technology) to determine the best path forward, as this same group has oversight of the EUA review process for PPE decontamination systems. These existing relationships allowed the team to quickly engage with the appropriate people in a meaningful way.

The first guidance document outlining the testing requirements for N95 mask reprocessing was released by FDA on 25 March 2020 (Enforcement Policy for Face Masks and Respirators During the Coronavirus Disease [COVID-19] Public Health Emergency). Based on the March 2020 guidance and the specific characteristics of the NovaSterilis technology, iFyber developed a comprehensive testing plan to address three main areas:

1. Demonstrate that the NovaSterilis process reduces viricidal activity by ≥ 3 logs and sporicidal activity by ≥ 6 logs on the N95 respirator material. Viricidal activity was evaluated using human coronavirus NL63 (a SARS-CoV-2 surrogate) in-house and the actual SARS-CoV-2 virus via a third-party BSL-3 lab that has been a long-term partner of iFyber. Sporicidal activity was evaluated using Bacillus atrophaeus.
2. Confirm that the materials used in the N95 respirators (i.e., filters and straps) are compatible with the NovaSterilis process and do not show excessive degradation or residuals. This included material characterization, mechanical strength testing, and quantification of sterilant residuals resulting from the NovaKill™ additive.
3. Provide evidence that decontaminated N95 respirators maintain adequate filtration, breathability, and fit performance for their intended use by HCP. For this requirement breathability and inward leakage were evaluated. Inward leakage is defined as the sum of two major components: filter penetration (leakage through the respirator filter material) and face-seal leakage (leakage of particles entering the respirator at the respirator-face interface).



This transmission electron microscope image shows SARS-CoV-2—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient in the U.S. Credit: NIAID-RML

TEST PLAN EXECUTION

When developing the test plan, in addition to meeting FDA guidance, it was important to consider the resources available, what tests could be performed by iFyber/NovaSterilis versus an external vendor, and what testing made the most sense for the NovaSterilis technology and specific application. Much of the testing could be managed and performed in-house in collaboration with the NovaSterilis team (e.g., validation of bioburden reduction, material and residual characterization, material /respirator compatibility); however, the iFyber network was engaged to provide resources that were not readily available. These established iFyber relationships allowed NovaSterilis access to the necessary equipment, facilities, and skills to complete the work with quick turnaround times using trusted partners.

For example, SARS-CoV-2 is a Biosafety Level 3 (BSL3) pathogen and requires specific containment and testing facilities. ZeptoMetrix Corporation (Buffalo, NY) was contracted to perform viral inactivation studies using the NovaSterilis platform within their BSL3 facilities. Similarly, Imperia Engineering Partners (Milford, MA) possessed the necessary equipment and expertise to complete elastic strap tensile testing. Local partners were also engaged, including Cornell University and Cayuga Medical Center, for the acquisition of test articles, coronavirus feasibility experiments, and initial respirator fit testing. To offset the significant backlogs encountered with vendors offering respirator performance testing, the appropriate fit/filtration test equipment was located, rented, brought in-house, and implemented by iFyber personnel.

To generate data in support of effectiveness claims and demonstrate a favorable risk-benefit ratio of the technology, iFyber worked collaboratively with NovaSterilis team members to quickly and efficiently mobilize the necessary resources, troubleshoot and overcome known limitations, and deliver quality results that met project and timeline objectives.

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PROPOSED WORKFLOW FOR HEALTHCARE FACILITY

As part of the pre-EUA submission, it was necessary to include a description of the chain of custody and safeguards implemented in the process to prevent inadvertent exposure of HCP and central sterile services department staff to contaminated devices. Small and mid-sized hospitals were engaged within the New York City area to ensure that appropriate controls were in place and the proposed workflow was consistent with current practices in hospital settings. Based on this information, the iFyber team drafted product labeling and instructions for use consistent with current central sterile processing best practices. These activities providing confidence that the process would adequately meet user needs.

NUMBER OF IFYBER PROJECT TEAM MEMBERS
6

PROJECT TEAM MEMBERS WITH PHDS
4

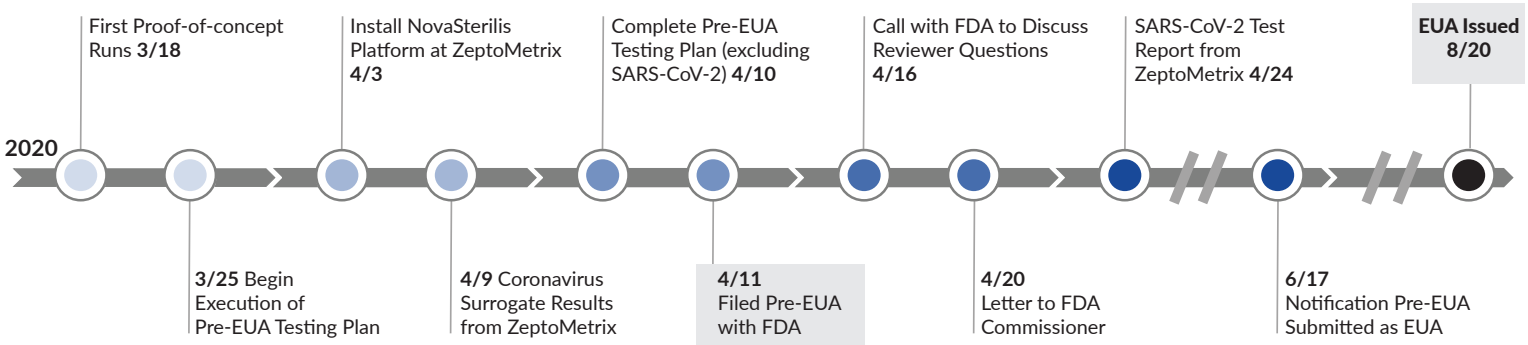
EXPERTISE IN MICROBIOLOGY, MATERIALS SCIENCE, CHEMISTRY, PROJECT MANAGEMENT, REGULATORY & QUALITY

PROOF OF CONCEPT TO PRE-EUA SUBMISSION
24 DAYS

TOTAL COST: $200,000

FDA FILING

Drafting of the Pre-EUA submission package occurred in parallel with testing to ensure the least amount of time between completion and filing. Testing was completed on 10 April (excluding SARS-CoV-2) and the pre-EUA was submitted to FDA on 11 April 2020 and the EUA was issued on 20 Aug 2020. As described above, the $scCO_2$-based platform is a novel sterilization methodology and there were numerous formal and informal requests for information or clarifications from FDA during the review period, which significantly lengthened the review time. At the time of writing, all other issued EUAs were for decontamination systems that utilized an established sterilization method. Although the bulk of the iFyber efforts occurred prior to the pre-EUA submission, the iFyber team continued to support NovaSterilis during these meetings and information requests and performed additional testing and investigations, on an as-needed basis. Further, in preparation for authorization, iFyber developed the appropriate quality and labeling documents to meet FDA reporting requirements and led the generation of collateral materials and scientific reports.



KEY SOLUTIONS

- As a result of iFyber's immersion and leadership, the time between the first proof-of-concept runs and pre-EUA submission was only 25 days
- iFyber seamlessly integrated with the existing NovaSterilis team and provided the necessary multi-disciplinary expertise to meet project and testing goals and address challenges as they arose
- iFyber's detailed project planning and quick and targeted execution allowed for optimal utilization of available resources – saving time and money
- iFyber was able to significantly accelerate the timeline because of their commitment to NovaSterilis' mission and the willingness to expose their strong network of contacts and collaborators

CONCLUSION

As demonstrated in this case study, iFyber provided a cost-effective, turnkey solution that was immediately implemented into NovaSterilis' current workflow. Within 24 days and for approximately $200,000, iFyber's multi-disciplinary 6-member team was able close the skills gap and efficiently work with NovaSterilis employees to take the project from concept to pre-EUA submission. Using this team-for-hire approach, NovaSterilis was able to address a new market opportunity with its technology that would have otherwise been lost.

SERVICES AVAILABLE

• Feasibility and efficacy testing across the areas of biology, chemistry, and materials science • Regulatory strategy development • Participation in FDA meetings and preparation and submission of regulatory filings • Quality Management System (QMS) development and Good Manufacturing Practice (GMP) consulting • Generation of publications, whitepapers, and collateral materials