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College Hall, University of Pennsylvania
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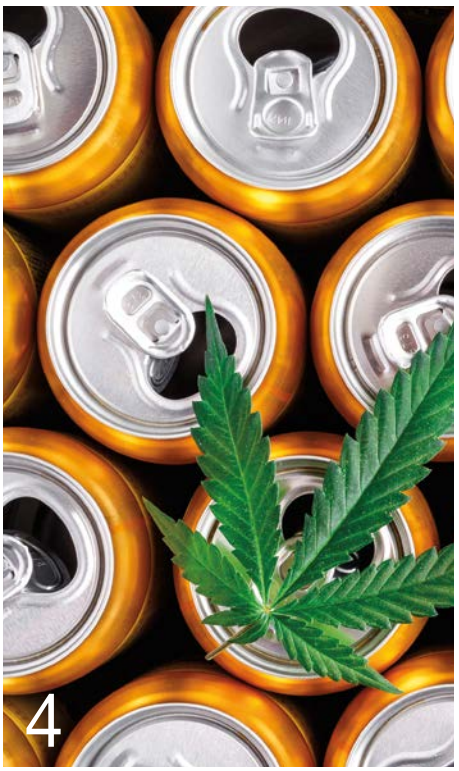

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Cannabis Chemistry: Mixing Buds and Beverages

By Kylie Wolfe

The beverage section at the supermarket is constantly evolving. Even though today's stores dedicate full aisles to different soft drinks, juices, and waters, the market is always welcoming new products. In recent years, consumers have become more concerned with health and wellness, swapping out sugary sodas for better-for-you beverages.

Alongside options with natural ingredients and fewer calories are dairy-free and plant-based alternatives. Next to those are energy and sports drinks that combine caffeine and electrolytes. Many companies have also started using more sustainable packaging. At the same time, an entirely new category is edging in — cannabis-infused beverages.

A Budding Industry

The cannabis beverage market is growing and, according to Grand View Research, is expected to be worth 2.8 billion USD by 2025. This accounts for expansion at a compound annual growth rate (CAGR) of 17.8 percent.[1]

As consumer interests change, several companies are stepping in to meet the demand for products in this category. In January 2021, Molson Coors introduced a line of cannabis-infused sparkling water in Colorado that's now available in 17 other states. The product was created alongside Truss CBD, a Canada-based beverage company. In November 2021, Bedfellows Liquid Arts, also in collaboration with Truss CBD, introduced two beer-inspired yet non-alcoholic cannabis beverages in Canada. Lagunitas also launched in this space with a zero-calorie, zero-carb option.[2]

"There are so many benefits to cannabis use and if we can package it in something that's already been socially ritualized, like a drink, it's that much easier to get into people's hands and to incorporate as part of their life and routine," said Ted Whitney, vice president of sales and marketing at Pacific Stone, a California-based cannabis company.

Cannabis Chemistry

Cannabidiol, or CBD, is a non-psychoactive chemical found in the cannabis plant. It can be used to treat anxiety and depression, stress, and inflammation, making it an attractive ingredient for health-focused consumers. That's where the beverage industry sees an opportunity.

But creating a cannabis-infused beverage is an involved chemical process. Bioactive compounds like terpenoids, flavonoids, and in this case, cannabinoids, aren't very soluble, and that's a challenge for manufacturers.[3]

"Cannabis extract is an oil that's inherently hydrophobic, so to get it to stay in solution is really challenging. Right now, the dominant paradigm is to put it into a nanoemulsion. You make little, tiny oil droplets and suspend them in water, but it's not super stable," said Whitney.

For example, after 90 days, the emulsion can fall apart and produce sediment. Because of the way cannabinoids are incorporated into an aqueous solution, they can also be less bioaccessible.

"The chemistry of cannabis is just not water friendly," he said. "Even when it goes into solution, your body doesn't absorb cannabis the same way without fats to encapsulate it."

Because the demand for cannabis-infused beverages is expected to rise, a result of more widespread consumer acceptance, there's not only a greater need for manufacturing solves, but for quality control and safety testing.

Navigating a New Category

Though legal in Canada, only a few states permit the sale of CBD-infused beverages, so navigating regulatory hurdles is also part of the process. But as the industry continues to grow, it should become easier to bring these products to market. For example, advancements in technology would help manufacturers better incorporate cannabinoids in drinks.

"Beverage consumption is something we've really normalized for people. They're very comfortable unwinding from work and cracking a beverage," said Whitney, who's also experienced in the craft beer space.

Even though there are still challenges to overcome, including plenty of social stigmas, industry professionals are ready to bring a new category to passionate consumers — and some are already doing so.

Kylie Wolfe is a Thermo Fisher Scientific staff writer.

1. No author listed. (January 2020). Cannabis Beverages Market Growth & Trends. Grand View Research. https://www.grandviewresearch.com/press-release/global-cannabis-beverages-market

2. Shoup, Mary Ellen. (November 2021). Molson Coors-backed Veryvell CBD sparkling water gains steam in evolving market. Food Navigator USA. https://www.foodnavigator-usa.com/Article/2021/11/22/Molson-Coors-backed-Veryvell-CBD-sparkling-water-gains-steam-in-evolving-market

3. No author listed. Accessed March 2022. The Art and Science of Cannabis Beverages. Le Herbe. https://www.newcannabisventures.com/wp-content/uploads/white_paper_ascb_v9.pdf

Multi-Attribute Method in Therapeutic Protein Manufacturing Quality Control

The Multi-Attribute Method (MAM) is an emerging quality control process that couples liquid chromatography and high-resolution accurate mass (HRAM) mass spectrometry.

Therapeutic proteins are a unique class of large-molecule drugs with much more complex structures than small-molecule drugs. During their manufacturing and storage, these proteins may be subject to chemically or enzymatically generated primary structure modifications. Specifically, post-translational modifications (PTMs) can contribute to the overall heterogeneity that becomes part of the product quality attributes (PQAs) of therapeutic proteins. Modifications that can affect the drug's efficacy and safety are classified as critical product attributes (CPQs) and must be monitored using various quality control (QC) processes.

One major advantage of MAM is that it can detect PTMs at the amino acid residue level, which is not possible using conventional profile-based methods of UV or fluorescence detection. The LC-HRAM-MS based MAM workflow involves initial enzymatic digestion of therapeutic protein to produce peptides of various length. This is followed by gradient separation using mobile phases with acetonitrile and water with either formic acid or trifluoracetic acid as modifiers. The HRAM MS analysis of the eluted peptides is used to determine the sequence

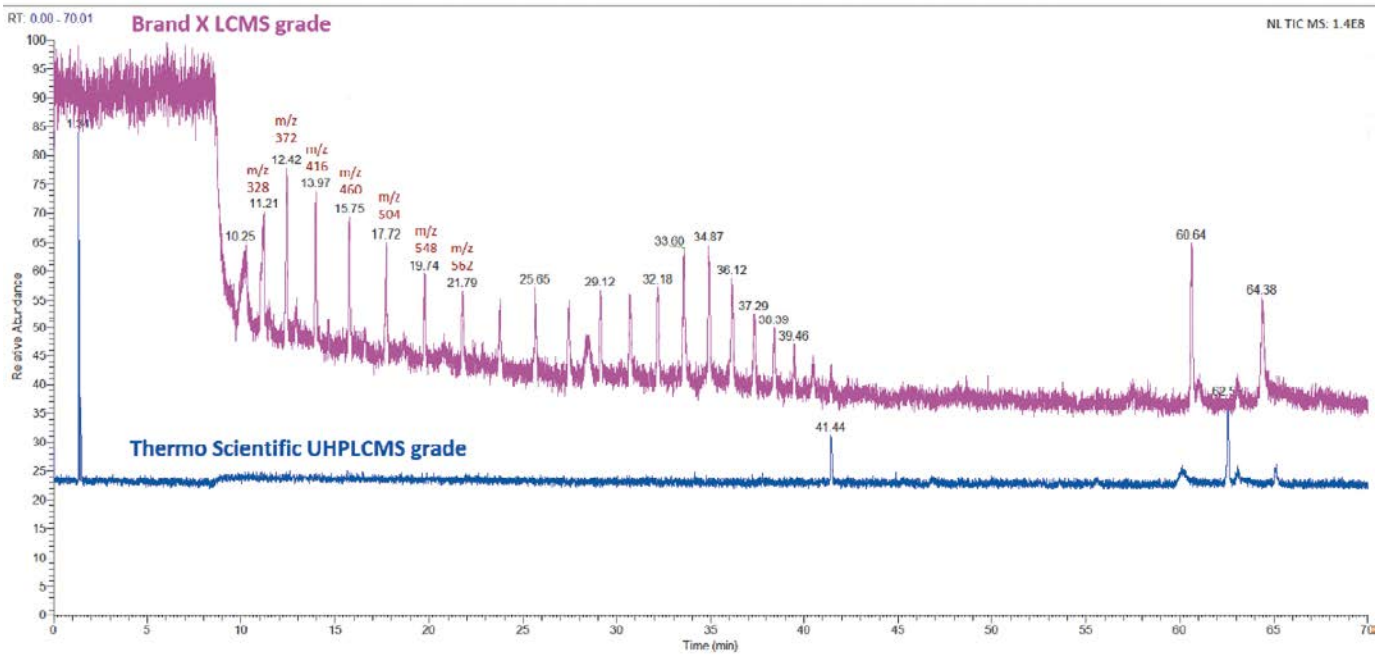

Figure 1. Control (blank) runs of an LC-MS MAM using two brands of LC-MS grade acetonitrile for mobile phases: brand X (top in pink) and Thermo Scientific (bottom in blue). The mobile phase is a binary gradient of 0.1% formic acid in water and 0.1% formic acid in acetonitrile. The m/z of seven peaks showing PEG-like +44 Da are labeled in brown.

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coverages that pinpoint the PTMs.

MAM must be robust and validated based on regulatory requirements to be useful for quality control methods in the biopharmaceutical industry. Moreover, the mobile phase solvents and reagents must be of high purity and without interfering contaminants. In a recently published study of MAM, more than 30 leading biopharmaceutical and LC-MS vendor labs cited chromatographic artifacts and contamination as two major causes of result abnormalities in peak detection.

Figure 1 shows an example of two control (blank) runs with mobile phases prepared from two different brands of LC-MS grade acetonitrile. Brand X has an elevated background that could compromise sensitivity and a repeating peak pattern that could severely interfere with peptide peak detection. The mass differences of 44 Da suggest PEG or PEG-like contaminants. All LC-MS grade solvents are not created equal, so solvents and reagents used for mobile phases must be evaluated before implementing MAM methods.

Thermo Fisher Scientific offers two grades of chemicals that are fully tested for LC HRAM MS MAM and other LC-MS analyses. Fisher Chemical Optima grade LC-MS solvents and blends are precisely mixed for lot-to-lot consistency and tested using LC-MS methods. Thermo Scientific UHPLC-MS grade solvents meet even more stringent specifications for assays that require more sensitivity.

Optima LC-MS grade and UHPLC-MS grade solvents and blends have been fully tested for low organic impurities including PEG-like substances. In the newly introduced Thermo Fisher Scientific MAM 2.0 workflow, UHPLC-MS grade acetonitrile and water are specified for preparing the mobile phase for the initial system performance evaluation test (SET).

Learn More About Thermo Fisher Scientific Chromatography Solvents

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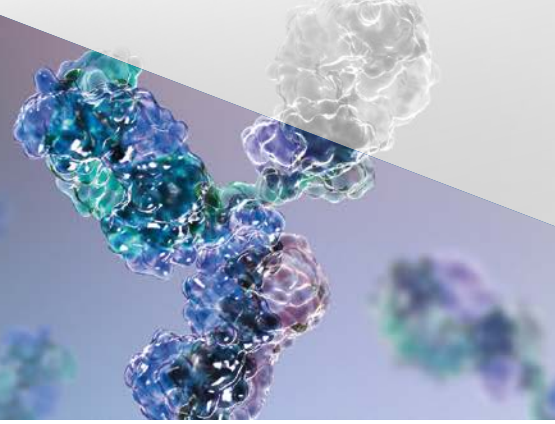

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Peptones in Bioproduction

Peptones have diverse and unique nutritional profiles that make them ideal components for creating robust, high-performance bioprocesses. They have been used for over a century to enhance diagnostic and bioproduction processes in microbial and mammalian systems.

As the bioproduction industry grew in the 1990s, Gibco peptones were used to replace serum, reduce risk, and significantly increase yields and overall process performance. Since that time, Gibco peptones have been used in more than 150 biopharmaceutical products and in developing biotherapeutics.

Peptone Composition and Role in Bioproduction

Peptones or hydrolysates are water-soluble products derived from the partial hydrolysis of proteins from yeast, plants, or animal sources. As a single supplement, they bring numerous advantages to cell culture, including nutritional diversity, protective effects, and performance enhancement.

Process Considerations

Media and supplements used in bioproduction processes typically fall into three broad categories: animal origin (AO), animal origin-free (AOF), and chemically defined (CD). All three support bioproduction, but each offers specific benefits that should be considered when determining suitability for an application or project.

AO processes may involve peptones derived from bovine, porcine, equine, and mixed or other animal tissues. AO peptone processes generally lend themselves to serum replacement, but this can prompt additional regulatory considerations and inherent variation.

AOF processes can produce similar benefits as AO processes but with less risk and fewer regulatory consequences. AOF peptones are derived from yeasts, plants like soy, cotton, wheat, and pea, and other non-animal sources.

CD processes involve components produced synthetically or derived from other specifically characterized and defined sources. One advantage of CD processes is the reduced regulatory risk that comes with knowing every component and its concentration. However, CD components vary, giving CD processes some inherent variability.

Understanding the relative advantages and considerations of each category of supplements is critical to monitoring and controlling processes.

Benefits of Peptones in Bioproduction

The unique nature of peptones makes them extremely useful components in bioproduction applications, and their multiple benefits can help you develop robust and high-performance processes.

• Versatility across cell types. The versatility of peptones is demonstrated by their successful use with many cell types, including yeast, bacteria, and mammalian cells.

• Nutritionally rich. Because each cell line and bioproduction process is different, it's important to screen multiple peptones at different concentrations to ensure optimal conditions.

Peptone Selection

To maintain process consistency, one must understand and control the sources of variability, which come from five main sources: biological factors, consumables, raw materials, process conditions, and environmental elements.

The two main considerations for peptone selection are supplier capability and process requirements. Understand your supplier's industry focus, testing capabilities, and willingness and technical ability to work with your process. Focus on peptones designed and tested based on bioproduction requirements. In addition to traditional testing, bioproduction peptones should be examined for solution clarity, endotoxin levels, mycoplasma presence, filterability, and other parameters. A supplier who understands the use of peptones in bioproduction can help increase the likelihood of a consistent and robust process.

Components added to your process may introduce trace contaminants. To achieve a consistent process, identify and control your component sources. A highly qualified bioproduction peptone supplier will offer advanced testing and documentation that meet your requirements.

Select a supplier that offers specialized analytical capabilities and can test complex media formulations to aid in process characterization and

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identification of critical components. Such analytical tools can aid in understanding sources of variability and enable controls and process optimizations to maintain consistency.

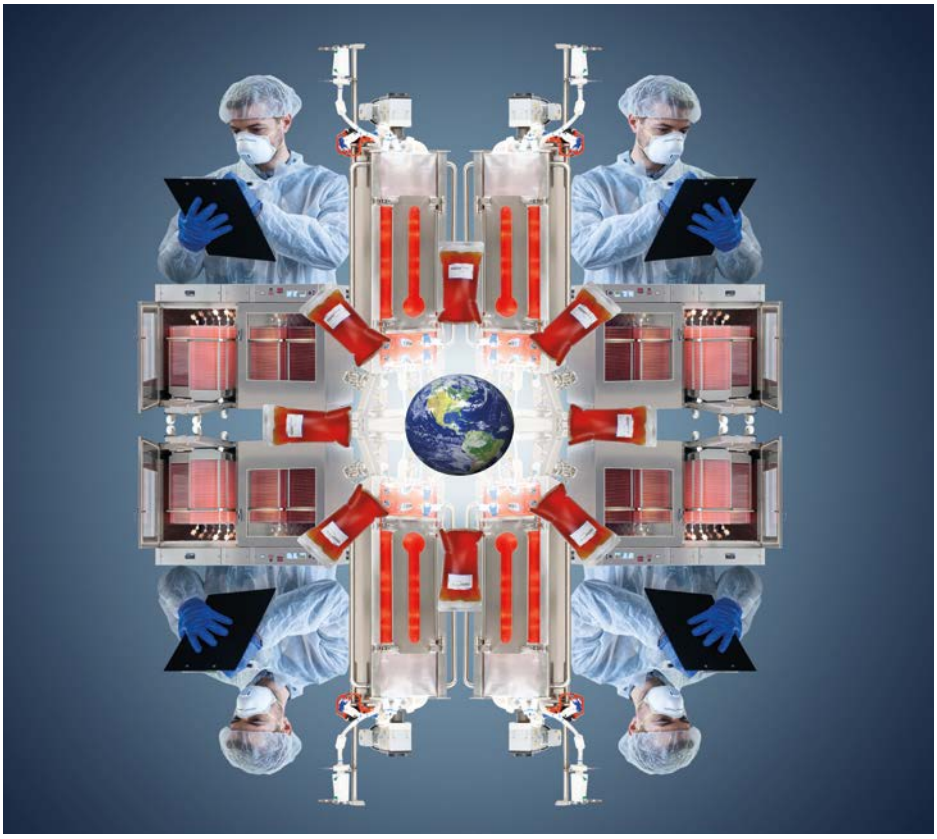
Equally important to supplier considerations is an understanding of the key requirements associated with using peptones in a bioproduction process. First, make comprehensive peptone screens a part of early medium development. Although peptones can be added at any point of that process — up to and through the bioreactor scale — adding them early in the process and optimizing with their presence generally improves process development outcomes.

Simplifying the Screening Process

Simplify peptone screening to identify the right peptone for your application. These suggestions may help you rapidly and efficiently select the peptones best suited to your process.

• Begin with a solid, established basal medium designed for your cell line. Optimized base media typically lead to faster, more successful results.

• Evaluate multiple products from the same peptone source substrate. Since peptones can have different compositions, screen more than one product to see which work best.



• Develop a thorough experimental design to evaluate various concentrations and consider both individual and blended peptone conditions. This approach can help you find the optimal peptones and concentrations.

• Characterize your process using different analytical techniques and establish baseline data by analyzing spent media. Investigate multiple lots of peptones and base media to identify potential sources of variability.

• Evaluate proliferation, production, protein quality, and other key attributes. Monitoring a single attribute is not likely to predict overall performance accurately.

• Identify key drivers of your specific bioproduction process and establish acceptable ranges to achieve the desired target performance.

A Proven Bioprocess Strategy

Peptones are well-established supplements in bioproduction with a proven record of success in pharmaceuticals currently on the market. The use of peptones in bioproduction processes provides a flexible, versatile, rapid, and efficient means of achieving desired targets within a wide range of cell types and methods.

For more information, visit **thermofisher.com/peptones**.

This editorial has been adapted from the September 2020 issue of BioProcess International.

mRNA Vaccines in the Fight Against Cancer

By Mike Howie

The COVID-19 pandemic and resulting vaccines from BioNTech–Pfizer and Moderna brought broad public attention to mRNA vaccines. While some were excited by the speed with which the vaccines were developed and their reported efficacy, others were skeptical of the technology. mRNA vaccines in general had never been implemented before, but they'd been in the works for more than 30 years.

Before the success of the COVID-19 vaccines, researchers studied mRNA vaccines for use against other viruses, including flu, Zika, rabies, and cytomegalovirus. Now, researchers are working on even more mRNA vaccines, targeting HIV, hepatitis C, malaria, tuberculosis, and others, according to Drew Weissman of the Perelman School of Medicine at the University of Pennsylvania.

But there's more: mRNA could even be used to fight cancer.

Vaccines as Cancer Treatment

The goal of the mRNA COVID-19 vaccines is to prevent, as much as possible, new infections. They don't help if the patient is already sick with COVID-19. mRNA cancer vaccines, on the other hand, would be used as interventions — they'd be given to patients who have been diagnosed with cancer as a treatment that teaches the immune system how to attack tumor cells. They would do this by prompting a potent cytotoxic T cell response, essentially equipping T cells with directions for killing cancer cells.

"What we're trying to do with the mRNA vaccine for cancer is alert the immune system to the tumor so the immune system will attack it," said John Cooke of the Center for RNA Therapeutics at Houston Methodist. "It's basically biological software."

For the vaccines to work, they have to tell the immune system what, exactly, to look for. The COVID-19 vaccines, for example, tell the immune system to look for a unique spike protein. But cancer cells and their DNA mutations vary from one patient to another, giving oncologists a moving target.

Personalized Medicine

To overcome genetic variations, mRNA cancer vaccines can be personalized for individual patients. First, doctors take samples of the patient's tumor and healthy cells, then use computers to compare the two and identify specific mutations present in the tumor. They can then design a molecule of mRNA that's used to create a vaccine, which trains the patient's immune system to recognize up to 20 mutations in cancer cells — then attack when it sees one. All of this is done in a span of four to eight weeks.

In some cases, however, the vaccine is not enough to successfully eliminate the cancer cells. So researchers are studying whether they can be combined with other treatments, such as chemotherapy, checkpoint inhibitors, or adoptive T cell therapy.

While the work is promising, it will likely be a while before mRNA cancer vaccines are commonplace. They'll require years of testing and clinical trials to ensure safety and efficacy, and so far, no trials have made it beyond phase II.

But if they succeed, they could become a powerful tool for treating patients who have cancer. And for people genetically predisposed to certain cancers, the vaccines could potentially be a preventative measure.

Mike Howie is a Thermo Fisher Scientific staff writer.

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Gibco peptones

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Gibco Starter Pak No. 2	Phytone Peptone, 100 g Difco Soytone, 100 g Bacto Yeast Extract, 100 g Bacto Proteose Peptone No. 2, 100 g Bacto Proteose Peptone No. 3, 100 g Bacto Casamino Acids, 100 g	**21-536-7**
Gibco Starter Pak No. 3	Bacto TC Yeastolate, 100 g Phytone Peptone, 100 g Difco Soytone, 100 g Bacto Yeast Extract, 100 g Bacto Malt Extract, 100 g Bacto Yeast Extract, Technical, 100 g	**21-536-8**

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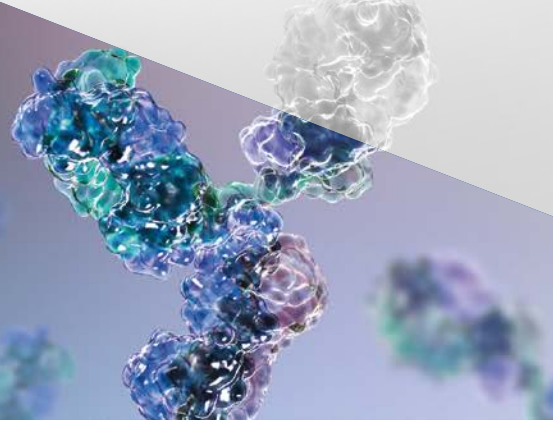

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Pipetting for a Lifetime: The Importance of Ergonomics

Pipetting is one of the most common and repetitive activities performed in laboratories throughout the world. Understanding the risks of injury and techniques and tools available to reduce that risk is important to lab personnel everywhere.

Risks of Injury

Ergonomics is the science of fitting the job to the worker. Poor ergonomics can result in musculoskeletal disorders (MSD) — injuries to muscles, nerves, tendons, ligaments, joints, cartilage, and spinal discs. Repetitive strain injury (RSI), a subset of MSD and a painful and sometimes permanent condition, is caused by repetition and excessive force.

Studies have found that laboratory personnel spend an average of two hours a day pipetting, a total of 500 hours a year. The same studies determined that more than 1.3 hours of pipetting activities per day increased the risk of injury.

Four main risk factors contribute to MSDs and RSIs: environment, posture, force, and repetition.

Environment and Posture

Pipetting takes place in a variety of work environments — at the lab bench, in manufacturing facilities, and in biosafety cabinets, clean environments, and other work areas. Wherever possible, remove impediments and arrange your workspace to create conditions conducive to good posture.

Force

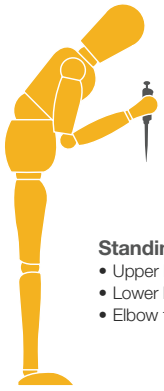
Manual pipetting requires force to grasp the pipette; attach pipette tips; depress, hold, and release the plunger; and eject the tips. Be aware of any pain in the hands, elbows, and shoulders from strained muscles and joints.

To help reduce pipetting forces:

- Regularly clean and lubricate pipettes
- Choose pipette tips that fit your pipettor correctly and eject easily
- Select pipettes that fit comfortably in your hand
- Find pipettes that require less plunger force
- Use electronic pipettes if your workload exceeds five microplates per day
- Opt for electronic pipettes with index finger action and electronic tip ejection

Bad posture

Seated posture:
- Shoulders elevated
- Upper arm elevated
- Elbow extended

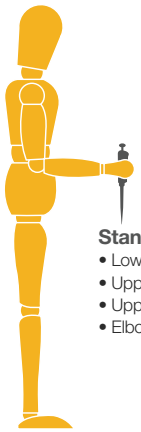


Standing posture:
- Upper back and neck stooped
- Lower back and trunk stooped
- Elbow flexed

Wrist posture:
- Wrist deviated

Good posture

Seated posture:
- Lower back supported by chair
- Upper back and neck upright
- Elbow bent at 90°
- Wrist in the same plane as the forearm



Standing posture:
- Lower back and trunk upright
- Upper back and neck upright
- Upper arm vertical
- Elbow bent at 90°

Wrist posture:
- Forearm parallel to the floor
- Wrist and forearm in the same plane

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Repetition

Pipetting is a repetitive activity, so reducing the number of individual and repeated movements can help reduce the risk of injury.

- For aliquoting, use a multi-channel or electronic pipette with mixing functions
- When using 384-well microplates, opt for a 16-channel or 384-well format pipette
- For processing more than five microplates per day, choose electronic pipettes with multi-dispensing functions
- Consider using an automated liquid handling device or reagent dispenser if your workload is 10 to 50 microplates per day
- For varying formats, replace single pipettes with multi-channel pipettes that have adjustable tip spacing

Thermo Scientific ClipTip Pipetting Systems

ClipTip Pipettes are used exclusively with ClipTip Pipette Tips to create an ergonomic liquid handling system. ClipTip technology provides:

- Extremely low tip attachment and ejection forces
- Comfortable use with low required force
- Complete tip seal on every channel
- Reproducible results between assays and users

F1-ClipTip Manual Pipettes

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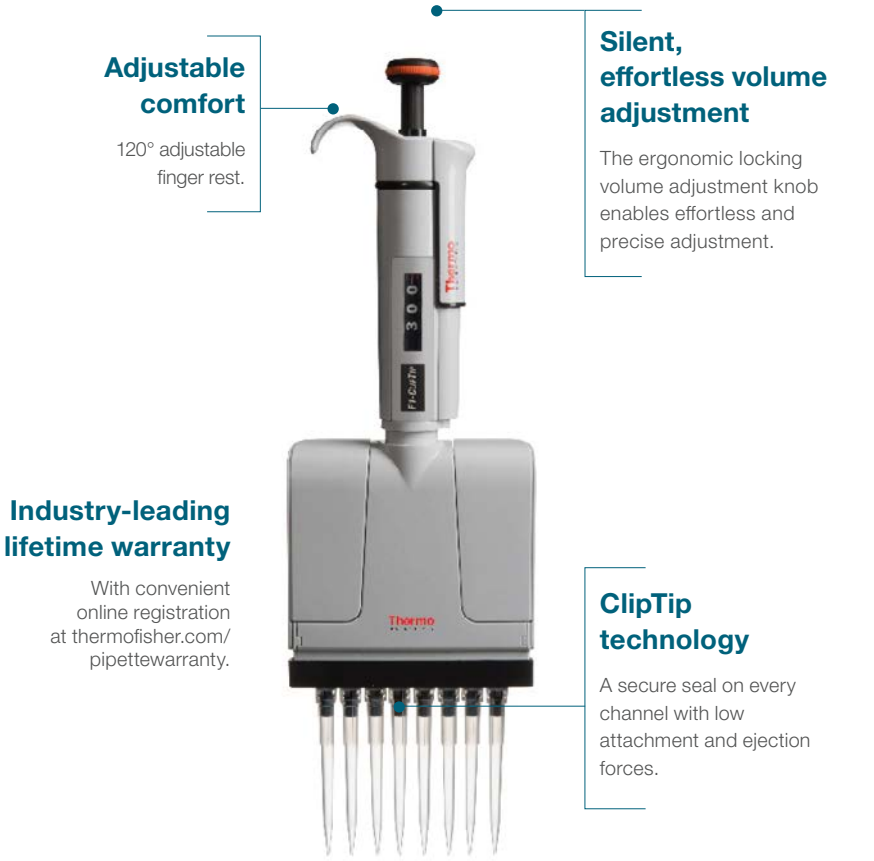
E1-ClipTip Electronic and Equalizer Pipettors

Switching from manual to electronic pipettes or automated dispensers can improve user comfort and reduce repetition and risk of injury.

Find E1 ClipTip Pipettes with volume ranges from 0.5 to 1,250 µL and with 8, 12, or 16 channels. Find E1 ClipTip Equalizer Pipettes with adjustable tip spacing with 6, 8, or 12 channels. Adjustable tip spacing lets you transfer samples between virtually any tube, rack, microplate, or horizontal gel box format.



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Tough Microorganism Lysing Bead Mill Tubes, 2 mL, 0.5 mm Glass Beads	50/Pack	**15-340-152**
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Zirconium Ceramic Oxide Beads, Dia.: 2.8 mm	325 g	**15-340-160**
Metal Beads, Dia.: 2.4 mm	500 g	**15-340-158**
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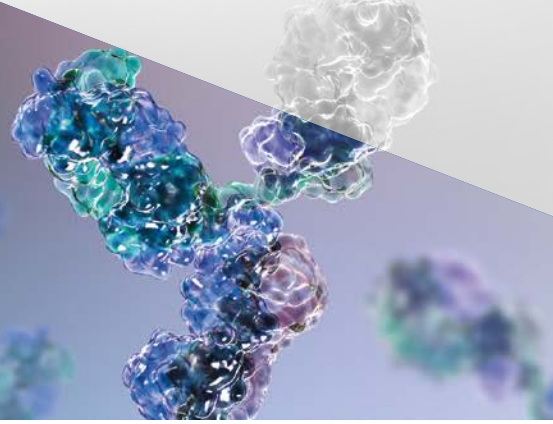

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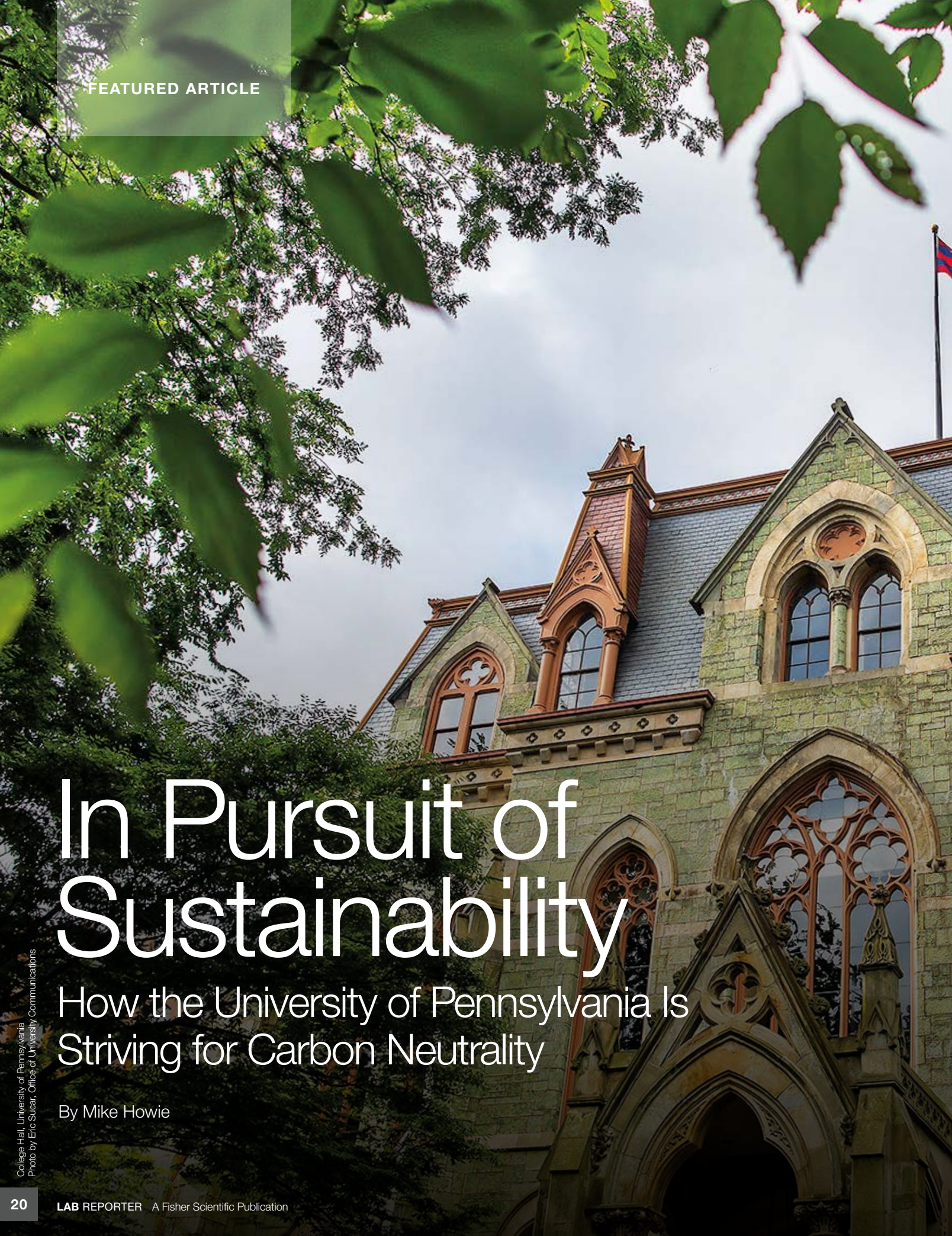

In Pursuit of Sustainability

How the University of Pennsylvania Is Striving for Carbon Neutrality

By Mike Howie

College Hall, University of Pennsylvania
Photo by Eric Sucar, Office of University Communications

Labs at the University of Pennsylvania recently spent three months competing against each other in all things cold storage management. Referred to as the Penn Green Labs Freezer Challenge, the event is an offshoot of the International Freezer Challenge, which is sponsored by My Green Lab and the International Institute for Sustainable Laboratories. It's one of Penn's many efforts to promote sustainable practices on campus.

The challenge encourages lab staff to develop positive habits like defrosting freezers, organizing samples, and tuning temperatures. There's a whole list of steps they can take to earn points, and at the end of the challenge, top scorers take home a prize. But there are no losers here — everyone becomes a little wiser, a little more sustainable.

That's the ethos Penn has developed over more than 13 years of steadily working to reduce its impact on the environment. What started with paper recycling has become a multi-faceted plan to reach carbon neutrality by 2042.

More Than a Decade of Progress

In 2007, former Penn President Amy Gutmann became the first Ivy League president to sign the American College and University Presidents' Climate Commitment. Two years later, the university published the first iteration of its Climate Action Plan, laying out the strategies it would use to reduce emissions of greenhouse gases across seven initiatives: academics, utilities and operations, physical environment, procurement, waste minimization and recycling, transportation, and outreach and engagement.

"This is a defining issue of the 21st century," President Gutmann wrote at the time. "At Penn, we must recognize the impact of a research institution of our size and acknowledge that our actions extend beyond our campus and have global consequences."

In the years since, sustainability efforts at Penn have spread from the Sustainability Office to a campus-wide culture of sustainable thinking and innovation among students, faculty, and staff. The university has created eight new environmentally focused academic centers, reduced building-related emissions by 41 percent, certified its main campus as a Level II Arboretum, adopted LEED Silver minimum building standards, reached a 21 percent diversion rate of waste going to landfills, and more.

Sustainability in the Lab

Among Penn's sustainability efforts is their Green Labs Program, which grew from one researcher's efforts to reduce waste and work more sustainably. There are now 12 labs committed to the program and a Green Labs Guide that lays out daily, monthly, and annual actions lab staff can take to reduce their environmental impact.

The Green Labs Guide also includes a checklist of individual steps lab staff can take to work more sustainably. Items include turning off biosafety cabinets and equipment when not in use, "chilling up" freezers, taking advantage of vendor recycling and take-back programs, repairing autoclave gloves before buying new ones, and scaling down procedures to use smaller amounts of hazardous chemicals, among others. Labs have even switched to reusable sharps containers and installed glassware washers to further reduce waste.

> "It's an urgent imperative that we continue to look at these things," Reardon said. "We can always do better, and we'll continue to attempt to do better."

They've also begun recycling masks and gloves through the TerraCycle Zero Waste Box program, which provides services to recycle waste that can't be recycled through regular municipal waste collection. The labs purchase a TerraCycle box — they're available for masks, gloves, eyewear, pipette tip boxes, and other common items — fill it with used products, then ship it out for recycling. To date, Penn has recycled more than 68,000 masks and gloves — more than any other organization in the United States, which amidst the COVID-19 pandemic and mask mandates has meant significant waste reductions.

University of Pennsylvania

continued from page 21

In Pursuit of Sustainability
How the University of Pennsylvania Is Striving for Carbon Neutrality

The Green Labs Program also encourages labs to choose equipment that reduces energy use. For example, the Ultra-Low-Temperature (ULT) Freezer Efficiency Program was established to reduce the number of old and under-utilized models by providing an incentive for purchasing highly efficient freezers, including models from the Thermo Scientific TSX line, and properly recycling freezers instead of sending them to the landfill.

Similarly, the university has a Green Fund that helps students, faculty, and staff secure funding for ideas that support objectives outlined in the university's Climate and Sustainability Action Plan 3.0, the most recent iteration of the plan that started in 2009. Applicants can receive up to 30,000 USD in funding, and those who are selected provide a full report of their project — including implementation procedures, results, and future recommendations — to the Penn Sustainability Office.

A Thoughtful Approach

Of course, some things in the lab need to remain consistent to ensure the accuracy and validity of scientific experiments, which the university prioritizes.

"We're not going to fundamentally change the chemicals or reagents or cell stacks that you're using," said Colleen Reardon, the university's senior director of strategic sourcing and sustainability. "What we want to do is say, 'In your research, what could be a more sustainable product or process than what you're using? Is there tubing that could be done with a product that's not as harmful to the environment? Have you looked for a place where we can recycle the glassware that you use?'"

Where products cannot be changed, sustainability efforts become more granular and consider the entire lifecycle of a product, from procurement to disposal. For example, can products be shipped with less packaging or more recyclable packaging? Can they be delivered from a more local source or on more efficient vehicles?

"It's top to bottom, not about the individual pipette tip," Reardon said. "Every single choice that everybody makes throughout the day in terms of a product they use can have a sustainability impact."

Setting an Example

Penn's approach to sustainability is all-encompassing — it places as much emphasis on small actions that individuals can take in the course of a normal day as it does on larger systemic changes that require years of effort and leadership support. And that breadth of focus has delivered more benefits than just reduced costs, emissions, and waste.

Encouraging people to walk or bike to campus helps reduce pollution while providing real health benefits. Installing refillable water stations cuts down on single-use plastics and encourages people to drink more water. Choosing to build and operate within sustainable guidelines helps the university secure grants from the federal government and private funders. And exposing students to a variety of sustainability efforts from the day they matriculate to the day they graduate produces new generations of leaders who view sustainability as a core responsibility.

Just as the university instills positive habits in its students, it serves as an example to its business partners and the broader community, demonstrating that sustainability and business are not at odds. In fact, they can support one another.

"It's good business," Reardon said. "If it's sustainable, then it's better for everyone in the long run, and you'll get a broader customer base and more customer loyalty, so it becomes a circular thing. We feel there's more to it than just our bottom line."

Indeed, sustainability is a critical factor in many aspects of life, one that requires continued focus and effort.

"It's an urgent imperative that we continue to look at these things," Reardon said. "We can always do better, and we'll continue to attempt to do better."

Mike Howie is a Thermo Fisher Scientific staff writer.

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Suspension or Adherent:
Which Cell Culture Method Is Right for Your Lab?

Your cell cultures are precious, and you want them to have the best growing conditions. So, when it's time to choose a cell culture method, should you choose an adherent or a suspension platform?

It depends.

The Options

The choice of a cell culture vessel is influenced by myriad operational and biological factors: scale, resources, timing, cell type, and how much — or how little — culture inspection and parameter control is required. Flasks and other adherent platforms are an entry point for many anchorage-dependent cell types, but they don't always support scale. Suspension platforms offer scalability, but adapting cells to grow in suspension can be challenging.

"It's not to say that one is particularly better than the other," said Hannah Gitschier, a Development Manager at Corning Life Sciences. "You have to consider what your goal is, as well as the constraints of your lab and cleanroom space, budget for capital equipment, and anticipated timelines to go from research to clinical trials and production scale."

Each method has pros and cons, and there are ways to get the best of both. Here's what you should consider.

Advantages of Adherent Cell Culture Methods

Flasks, roller bottles, and other vessels for adherent cell culture offer ease of use and the option to provide anchorage-dependent cell types with biologically relevant surfaces.

"Most tissue-derived cells in the body require a surface or extracellular matrix to support growth and normal proliferation," Gitschier said. "Adherent cell culture platforms provide scalable options with increasing cell growth surface areas for production and the option to utilize specialty surface chemistries and coatings that mimic a local microenvironment."

Adherent platforms may also have the benefit of visualization. Using an inverted microscope, you can view growth on flask surfaces or the bottom layers of stacked vessels.

"There are certain cell types where morphology is critical to indicating things beyond just cell health," Gitschier said. "If you have multipotent or pluripotent stem cells that are subject to spontaneous differentiation, being able to see them is a really important way to catch problems early."

These and other advantages make adherent methods a natural choice for many vaccine, cell therapy, and gene therapy programs, which tend to be based on anchorage-dependent cell types. Adherent cultures also give the gift of time, a significant benefit for startups racing to get into the market.

"If there's steep competition to be the first to market, time could be one of those high-stake factors," Gitschier said. "If you already have an adherent-based system being utilized for the development and production of other regulatory-approved therapies, and you know how to scale quickly, it might be to your benefit to stick with the same proven platforms to get through clinical trials and approvals."

Advantages of Cell Suspension Culture Methods

Suspension method vessels range from small-scale Erlenmeyer and spinner flasks to large-scale stirred-tank bioreactors. For these approaches, the value is simple: You get yield scale. A lot of it.

That scalability and control makes suspension platforms an attractive option for manufacturers who want to gain operational efficiency. But the trade-off could be more work up front. Researchers must adapt anchorage-dependent cell types to suspension environments. That takes time and effort.

"Anchorage-dependent cells might suffer from growth reduction and lower yields during adaptation," Gitschier explained. "And the shear forces and stresses that occur in suspension culture are detrimental to many cell types, but especially anchorage-dependent primary and stem cells."

Cell suspension cultures also lack the benefit of direct visualization, although you can still monitor progress using other indicators as well as on-line and in-line process controls.

"You still have ways of monitoring cell growth, like pH acidification and oxygen and glucose consumption," said Angel Garcia Martin, PhD, MBA, a business development manager at Corning Life Sciences. "Those are indirect measurements of culture growth, but you do lose the ability to look at the cells under a microscope."

Suspension cultures can produce the high volume of cells needed for applications,

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despite the challenges. The production of monoclonal antibodies using Chinese hamster ovary (CHO) cells is a classic example. Researchers adapted these cells to thrive in a suspension environment, and it has become the primary method of production.

However, not every program needs that kind of scale. Autologous therapies and gene therapies targeting rare diseases or small patient population sizes may be produced sufficiently at smaller scale.

Get the Benefits of Both

You can maximize the benefits of each method with next-generation technologies. Get more growth surface area within smaller and more manageable adherent culture vessels or reduce shear stress levels in suspension cell cultures.

That's the idea behind Corning HYPERStack vessels, which add more layers into the same footprint as CellSTACK cell culture vessels while maintaining adequate gas exchange.

Microcarriers let you scale with even greater surface area-to-volume ratio and offer pH and gas control with stirred-tank reactors. Taking it to the next level, fixed-bed bioreactors and the emerging technology of Corning Ascent Fixed Bed Reactor systems increase the surface area-to-volume ratio while also immobilizing the cells to mitigate the risks of shear stress.

"When you start out, flasks or stacked vessels are a preferred option," Garcia Martin said. "Once you start growing, and need to achieve production scale, there's a huge labor and clean room space cost advantage to going with a fixed-bed bioreactor."

In the end, Gitschier and Garcia Martin agree: The method depends on your needs.

"There are certainly different benefits to different technologies, depending on your resources, scale, visualization needs, automation requirements, and whether shear stress can be managed or is detrimental to the culture," Gitschier said. "It's really about identifying what you want to get out of your platform and working from there."

But you don't have to make the decision alone. Consult with your equipment or culture vessel manufacturer or supplier. Their field application experts can help you determine which solution may best support your end goals based on their experiences with similar labs and applications.

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FB-11207	12.75 L	(3.3 gal.)	**FB11207**
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The Challenges of Qualifying Packaging Systems

Frank Butch, Engineering Manager, Sonoco

Temperature-assurance packaging (TAP) is typically qualified using minimum and maximum amounts of a specific product or product type and with a standard shipping method or distribution channel. After qualification, changes to specifications only occur if and when qualification testing is repeated.

However, this approach can be limited. That's why Sonoco ThermoSafe TAP products are qualified using the most challenging conditions.

The Limits of Pre-Qualification

Pre-qualified TAP shippers available to customers may not always be tested using a specific representative product volume.

- Large payloads will more slowly change temperatures in response to the ambient temperature exposure; smaller payloads will respond more rapidly
- Ambient temperature profiles used for testing may not represent the actual shipping method
- Differences between expected and actual temperature ranges may result in more expensive over-developed systems or poorly performing under-developed systems

Temperature probe placement during testing is determined by the manufacturer, but every TAP container also has its own temperature gradient. This can result in pre-qualified shippers that have not been physically exposed to the extreme temperatures possible with alternative shipping methods.

Testing Parameters and Methods

When measuring thermal properties, air temperature is most difficult to test. Air has a significantly greater thermal diffusivity than other materials — it responds rapidly to changes in ambient temperature but has little ability to retain any absorbed heat. A worst case for evaluating product volume would be an empty product carton, where an extremely small mass (air, for example) occupies a large volume. We use a corepack filled with product cartons (which are filled with air) to measure the effects of various fill materials or dunnage that impact airflow within each shipping system.

Results

In parcel shipper testing, conduction is the dominant heat transfer mode, but convection becomes more important with increases in the size of the shipper and product load. Preliminary testing data show that the coldest cold probes and the warmest warm probes in every testing configuration were found in shippers using air as the product and only cartons as dunnage. As expected, temperatures within these shippers changed more rapidly than with other configurations.

Benefits

We have found that qualifying our TAP using air as the product load solves several challenges. Since air temperature changes the most rapidly, this provides a more conservative estimate for containers that contain vials, syringes, medical devices, or other contents. This method also eliminates the need to acquire actual product to conduct thermal qualification, since the worst-case scenario has already been considered.

Sonoco ThermoSafe is a global leader in temperature-controlled packaging and innovative cold chain solutions for the safe and efficient transport of pharmaceuticals, biologics, vaccines, and other temperature-sensitive products.

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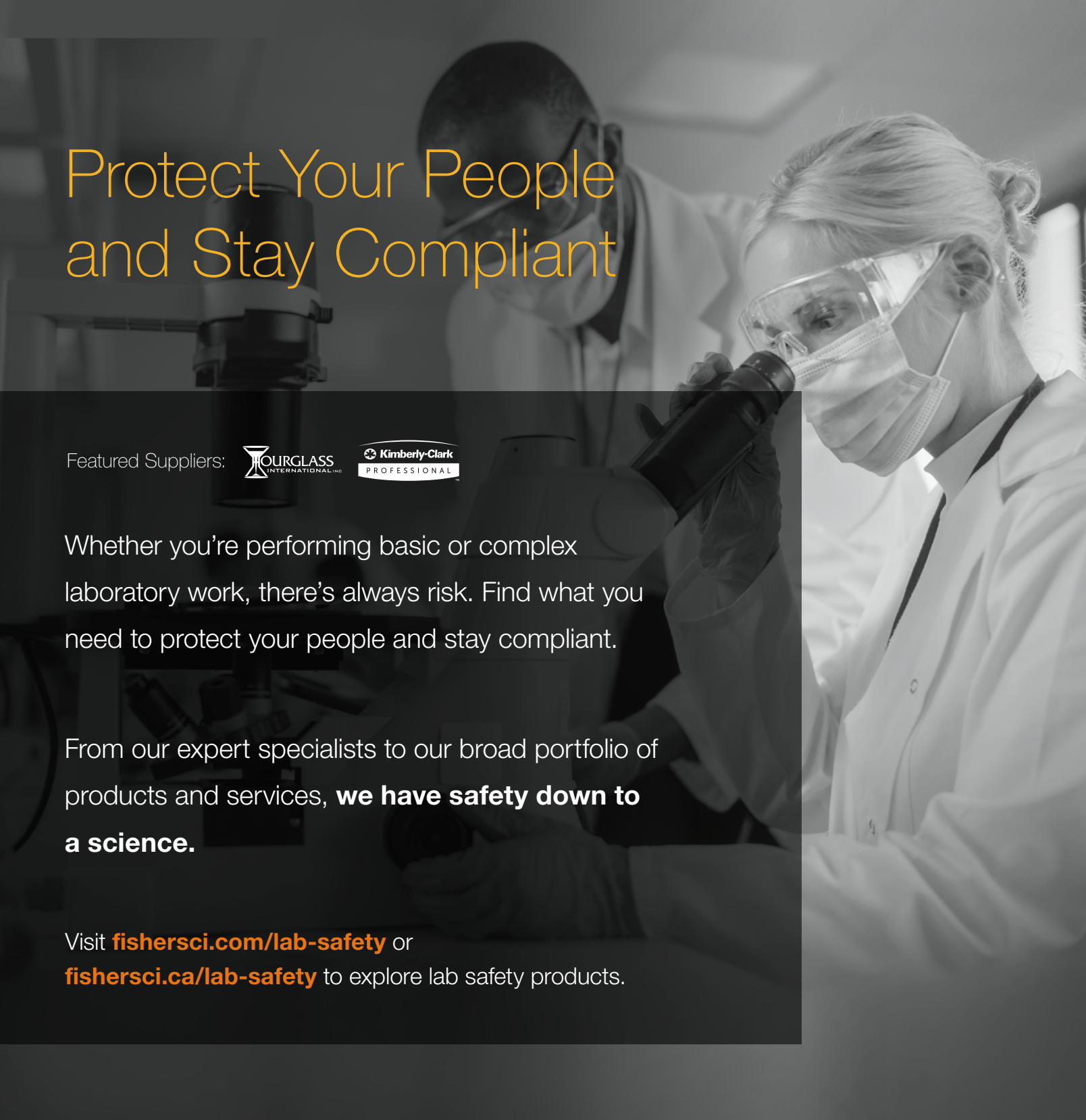
KB ECO 1020	36 cu. ft.	45.3 x 75.8 x 45.3 in.	**08-112-076**



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Lithium-Ion Battery Recycling

to Play a Key Role in Reducing Greenhouse Gas Emissions

By Mark Miller

Even for people fully aware of the growing threat greenhouse gases pose to the environment, the recent numbers are eye-opening: The transportation sector alone produced about 7.3 billion metric tons of CO_2 emissions worldwide in 2020. Passenger cars were the largest source, accounting for 41 percent.[1]

It was startling statistics like these that drove an alliance of governments, auto manufacturers, financial institutions, and others during the 2021 United Nations Climate Change Conference (COP26) to establish a goal of selling 100 percent zero-emission cars and vans by 2040. In a separate agreement, 15 countries also expressed their intention to transition to sales of 100 percent zero-emission trucks and buses by 2040.

These types of agreements signal a growing wave of electric vehicles (EVs) coming to market, along with corresponding demand for the lithium-ion (Li-ion) batteries that power them. But will there be enough metals — lithium, cobalt, nickel, and others — to produce the needed Li-ion cells? Materials scientists are working on recycling technologies to help keep pace with demand.

ReCell Ramps Up

The U.S. Department of Energy (DOE) responded to the need for Li-ion battery recycling in 2019 and launched the ReCell Center for research and development. Located at Argonne National Laboratory, ReCell collaborates with other labs, universities, manufacturers, and participants in the Li-ion battery supply chain. One of its goals is to develop a cost-efficient recycling process to recover high-value materials for sale back to manufacturers.

Cost-efficient techniques are important because they provide Li-ion recycling projects with economic viability and sustainability. In fact, ReCell aims to help grow an entire battery recycling industry through economic and environmentally sound recycling processes.

"This center will create jobs and create a national supply of lithium-based battery materials, as well as spur the adoption of an affordable electric vehicle economy," said Daniel R. Simmons, assistant secretary of the DOE's Office of Energy Efficiency and Renewable Energy, in the *Design News* article, "Volkswagen, DOE Want EV Battery Recycling for Fun and Profit."

Makers' Marks

Auto and battery manufacturers are setting more ambitious sustainability targets, too. Volkswagen has opened a battery recycling plant at its factory in Salzgitter, Germany. "For 10 years now, we have been researching how we can recuperate raw materials. These include, above all, cobalt, lithium, manganese, and nickel," explained Thomas Tiedje, head of technical planning at VW, in the same *Design News* report.

EV innovator Tesla claims it has a process that can save up to 92 percent of the elements that go into a battery pack, according to the article, "New Tesla Battery Recycling Process Reportedly Produces No Waste," in *InsideEVs*. And a spokesperson from a subsidiary of China's biggest maker of Li-ion cells says it can recycle 120,000 metric tons of batteries per year — enough for more than 200,000 cars, reports Davide Castelvecchi in his article, "Electric cars and batteries: how will the world produce enough?" in *Nature*.

Timing Is Everything

These efforts may be coming just as they're needed. EV sales more than doubled in 2021 to reach 6.6 million. That's nearly 9 percent of the global car market and more than triple their market share from just two years earlier.[2] To meet the zero-emissions goals of agreements like those announced at COP26, Li-ion battery recycling needs to mature with the burgeoning EV market.

This level of growth requires a re-evaluation of Li-ion battery metal sources. According to Castelvecchi's report, there may be enough lithium to support the transition to EVs up to 2050. Cobalt, however, could face shortages due to the conditions in which it is mined and other factors. Nickel shortages may also arise. These constraints — along with the demand for Li-ion power from a range of devices and emerging energy storage systems (ESSs) — could make Li-ion battery recycling a critical capability for achieving a zero-emissions future.

Mark Miller is a Thermo Fisher Scientific staff writer.

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2. Paoli, L. & Gül, T. (2022, January 30). Electric Cars Fend Off Supply Challenges to More Than Double Global Sales. International Energy Agency. https://www.iea.org/commentaries/electric-cars-fend-off-supply-challenges-to-more-than-double-global-sales

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Greiner Bio-One CELLMASTER Roller Bottles

CELLMASTER sterile roller bottles are available in short and long forms. The smooth inner surface is treated for better cell culture adhesion.

- Growth area: 850 cm^2
- Smooth, TC-treated polystyrene
- HDPE plug seal or filter screw caps
- Filter membrane pore size of 0.2 µm to help protect against contamination
- Endotoxin testing tolerance level of 0.03 EU/mL

CELLMASTER bottles are also available with or radially ribbed inner surfaces to increase growth area.

Form (Capacity)	Growth Area	Cap Type	Mfr. No.	Quantity		Cat. No.
Short (2100 mL)	850 cm^2	Filter	680045		48/Case	**07-000-347**
	850 cm^2	Plug Seal	680048		48/Case	**07-000-730**
Long (2520 mL)	850 cm^2	Filter	680058	2/Pack	24/Case	**07-000-346**
	850 cm^2	Filter	680068		24/Case	**07-000-732**
	850 cm^2	Plug Seal	680060	2/Pack	24/Case	**07-000-344**
	850 cm^2	Plug Seal	680065		24/Case	**07-000-731**

Online Chromatography Resources to Help You Separate with Success

The Fisher Scientific channel brings you chromatography products and information to support your methods and workflows. Our online resource centers make it easy to find exactly what you need no matter your application.

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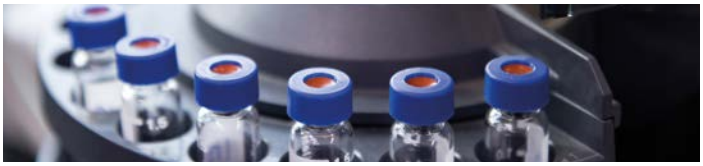

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Fisherbrand Sonic Dismembrators create energy that is transmitted through a titanium probe into a liquid sample to create cavitation (the implosion of micro-bubbles with high shear forces).

Each Fisherbrand Sonic Dismembrator includes a generator, converter, cables, wrench set, and one probe. Other probes and accessories, including the stand and clamp shown here, are sold separately.

Model 505

Model	Applications	Capacity	Power	Cat. No.
50	• Basic Cell Disruption	0.2 to 50 mL	50 w	**FB50110**
120	• Cell Disruption • Protein Extraction • DNA Shearing/ChIP	0.2 to 50 mL	120 w	**FB120110**
505	• Cell Disruption • Nanoparticle Dispersion • Homogenization/Mixing	0.2 to 1000 mL	500 w	**FB505110**
705	• Cell Disruption • Protein Extraction • DNA Shearing/ChIP • Nanoparticle Dispersion • Homogenization/Mixing • Sonochemistry	0.2 to 1000 mL	700 w	**FB705110**

CleanSpace Joins WHO in Call for a Revolution in Respiratory Protection

An immediate shift from single-use PPE to reusable solutions in healthcare settings is urgently needed.

Global respiratory protection specialist CleanSpace Technology stands firm with the World Health Organization (WHO) in calling for reform in PPE procurement. Staggering figures were recently released about the amount of consumable waste produced due to COVID-19. Today's technology can deliver reusable and more sustainable solutions for healthcare organizations, offering long-term cost savings and reliable protection for healthcare workers.

In February 2022, the WHO released a report titled *Global analysis of health care waste in the context of COVID-19: status, impacts, and recommendations*. This report estimates that 87,000 metric tons of PPE was procured between March 2020 and November 2021 — most of which is likely to have become waste.

The report references a recent U.S. study that found that replacing every disposable mask used in patient interactions in the first six months of the pandemic with reusable respirators would have reduced waste by 69 million kilograms and saved 4.9 billion USD.[1]

The WHO report notes that changing behavior in favor of reusable solutions requires focused effort from dedicated leadership — starting with multilateral institutions like WHO, UNICEF, the Global Fund, Gavi, and the World Bank — that advises at the global level on the use and procurement of PPE.

CleanSpace welcomes this report as a huge and positive step in the PPE conversation. Along with the environmental issues, this reliance on low-performing single-use masks also affected healthcare worker infection rates, staff shortages, and other health and social problems.

"Healthcare worker protection is paramount to maintaining viable care networks — sustainable respirator solutions exist and are readily integrated into healthcare workflows," said Dr. Alex Birrell, CleanSpace Technology CEO. "Not only are PAPRs reusable, but they are also the gold standard for high-risk airborne contagions."

Product Information

The NIOSH-approved CleanSpace HALO was designed specifically for healthcare, pharmaceutical, and laboratory personnel and features:

- P100 HEPA filtration (99.97%)
- Low weight (less than one pound)
- No belts or hoses
- Smart CleanSpace AirSensit Technology
- Simple and fast donning
- IP Rated 66 water tolerance
- Reusable, cost-effective design
- Award-winning design and protection: Red Dot (Product Design & Innovative product) and OH&S (Platinum Respiratory Protection)

Use the CleanSpace Smart app to check your HALO battery level, mask fit, and more. You can download the app for free from the Apple App Store and the Google Play Store.

CleanSpace Technology is an Australian company that designs and manufactures next-generation respirators. The proprietary technology at the heart of all CleanSpace respirators was designed by ex-ResMed biomedical engineers. The company assists in product training, fit testing, and instruction for maintenance and care.

1. Chu J, Ghenand O, Collins J, Byrne J, Wentworth A, Chai PR, et al. Thinking green: modeling respirator reuse strategies to reduce cost and waste. BMJ Open. 2021;11(7):e048687. doi:10.1136/bmjopen-2021-048687.

Content provided by:

CleanSpace® RESPIRATORS

Description	Size	Quantity	Cat. No.
HALO Half Mask	Small	Each	**17-800-647**
	Medium	Each	**17-800-648**
	Large	Each	**17-800-649**
HALO Full Face Mask	Small	Each	**17-800-650**
	Medium/Large	Each	**17-800-651**
HALO Neck Support (Non-Fabric)	Small	Each	**17-800-658**
	Large	Each	**17-800-659**
HALO Power System NIOSH, Includes Respirator, Neck Support, HEPA Filter, Charger	NA	Each	**17-800-646**
HALO Particulate Filter, HEPA, Low Profile	NA	3/Pack	**17-800-652**
HALO Cleaning and Storage Plug Set	NA	Each	**17-800-654**
HALO Head Harness for Half Mask (Non-Fabric)	NA	Each	**17-800-657**
HALO Station Charging and Storage Case	NA	Each	**17-800-653**

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More Sustainable Science

MilliporeSigma

MilliporeSigma Milli-Q Laboratory Water Systems

Compared to previous-generation water purification systems, the Milli-Q IQ 7 series has been designed to reduce water and energy consumption, minimize the use of plastic, and eliminate chemical waste while providing consistent pure and ultrapure water.

- Less water usage: Reverse osmosis (RO) purification
- Lower energy: Hibernates during periods of inactivity
- No chemical waste: Electrodeionization, not resin; mercury-free UV lamps
- Fewer disposables: Extended cartridge life (one year vs. six months)
- Less materials: Smaller system component dimensions

Description	Cat. No.
IQ 7000 System, Production Flow Rate: 2 L/min.	**ZIQ7000T0C**
IQ 7003 System, Production Flow Rate: 3 L/min.	**ZIQ7003T0C**
IQ 7005 System, Production Flow Rate: 5 L/min.	**ZIQ7005T0C**
IQ 7010 System, Production Flow Rate: 10 L/min.	**ZIQ7010T0C**
IQ 7015 System, Production Flow Rate: 15 L/min.	**ZIQ7015T0C**
IQ Storage Tanks, Capacity: 25 L	**TANKA025**
IQ Storage Tanks, Capacity: 50 L	**TANKA050**
IQ Storage Tanks, Capacity: 100 L	**TANKA100**

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Capacity	Mfr. No.	Quantity	Cat. No.
0.5 to 10 µL	F174101	960/Pack	**F174101G**
1 to 20 µL	F174201	960/Pack	**F174201G**
10 to 200 µL	F174301	960/Pack	**F174301G**
100 to 1000 µL	F174401	960/Pack	**F174401G**

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SLi3PRO


SLi6PRO

Model	Illumination	Objectives	Cat. No.
SLi3PRO	Fluorescence	Infinity LWD Plan Fluorescent Objective (4X, 10X, 40X)	**SLI3P-FL1**
	Phase Contrast	Infinity LWD Plan Achromatic Objective (4X) and Positive Phase Contrast (10X, 20X)	**SLI3P-PH1**
	Phase Contrast and Fluorescence	Infinity LWD Plan Fluorescent Objective (4X, 10X) and Infinity LWD Plan Positive Phase Fluorescent Objective (20X, 40X)	**SLI3P-FLP**
SLi6PRO	Fluorescence	Infinity LWD Plan Fluorescent Objective (4X, 10X, 40X)	**SLI6P-FL1**
	Phase Contrast	Infinity LWD Plan Positive Phase Contrast Objective (4X, 10X, 20X)	**SLI6P-PH1**
	Phase Contrast and Fluorescence	Infinity LWD Plan Positive Phase Contrast Objective (4X, 10X) and Semi-Apo Infinity LWD Plan Positive Phase Contrast Objective (20X, 40X)	**SLI6P-FLP**

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*Patent www.LowDerma.com/patents

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Size	Packaging	Mfr. No.	Cat. No.	Size	Packaging	Mfr. No.	Cat. No.
XS	100/Pack, 1,000/Case	500	**17-900-927**	L	100/Pack, 1,000/Case	503	**17-900-930**
S	100/Pack, 1,000/Case	501	**17-900-928**	XL	100/Pack, 1,000/Case	504	**17-900-931**
M	100/Pack, 1,000/Case	502	**17-900-929**	XXL	90/Pack, 900/Case	505	**17-900-932**

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Model	Application	Ultimate Vacuum	Flow Rate	ATEX Compliant	Integral Gas Ballast Valves	Cat. No.
N 96	Filtration, SPE, Aspiration	97.5 torr, 130 mbar	7 L/min.	No	No	**13-880-904**
N 820 G	Rotary Evaporation, Degassing, Fluid Aspiration, Centrifugal Concentration, Vacuum Oven, Gel Drying	4.5 torr, 6 mbar	20 L/min.	Yes	Yes	**13-880-905**
N 840 G	Rotary Evaporation, Filtration, Centrifugal Concentration, Vacuum Oven	4.5 torr, 6 mbar	34 L/min.	Yes	Yes	**13-880-906**

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