

Whitepaper (Human created & curated content)

Increase Your Profit Margin with Lyophilization

Benefits for Reagent Kits & Diagnostics

By Wayne Woodard

OVERVIEW

Lyophilization is a hot topic in biotech and pharma, as numerous suppliers are introducing lyo-ready or pre-lyophilized products to the marketplace. As a result, demand for lyophilization services is growing at a rate that exceeds the current number of trained experts. Benefits of lyophilized products include reduced refrigerated warehouse requirements, lower shipping costs, simplified product use, and longer shelf life. The future of lyophilization continues to balance higher upfront costs versus long-term benefits as improvements in conventional lyophilization technology efficiency are sought. If your product uses cold chain logistics, requires user pipetting, or has a short expiration window, there are significant benefits to introducing a lyophilized version.

COST SAVINGS

One of the greatest benefits of lyophilization is the ability to reduce expenses on multiple levels. Lyophilized products are shelf stable at room temperature; reducing electrical, space, and equipment costs during storage. According to the Healthcare Distribution Alliance (HDA), 49% of warehouse volume is [used to store refrigerated or frozen products](#)¹, so removing cold storage needs significantly reduces warehouse requirements. Additionally, Good Distribution Practices (GDPs) are becoming more broadly adopted, which [increase costs to monitor temperature range storage](#)¹ compliance for cold products.

While the cost savings from room temperature storage are significant, those attributed to cutting cold chain shipping logistics may be even greater. In 2018, the pharmaceutical coldchain logistics industry was valued at [over \\$15 billion and is predicted to expand to \\$18 billion by 2022](#)¹. Of that \$15 billion, \$10.6 billion is transportation costs and \$4.4 billion is packaging related. Consider how much money is wasted by cold chain packaging. Over-packing wastes resources and fuel, and adds to transportation costs, while under-packing leads to damaged or spoiled product that must be [replaced](#)². Using lyophilization to replace your cold chain with room temperature shipping can dramatically bring down costs across multiple categories.

“The benefits of lyophilized products include reduced refrigerated warehouse requirements, lower shipping costs, simplified product use, and longer shelf life.”

EASE OF USE & EXTENDED SHELF LIFE

There are additional, less obvious savings from lyophilization including reductions in product replacements and write-offs. Unit-dose beads (such as [LyoDose™](#) beads) can eliminate pipetting steps and simplify protocols for your end user. For example, consider the difference in complexity between pipetting three varying reagent volumes from three tubes versus simply adding three uniquely colored beads (fig 1) to a pre-filled reconstitution tube. Reducing user error conserves reagents, sample, and time for customers. Switching to lyophilization can also prevent costly replacement expenses and service calls. With some lyophilized products boasting expiration times of up to twenty years, lyophilization can extend your product's lifespan, reducing write-offs due to expiry. Overall, the costs of lyophilization are minimal compared to the savings.



Fig 1. Example of LyoDose bead color-coding

ENVIRONMENTAL RESPONSIBILITY

Another hidden benefit of lyophilization is the positive impact on the environment. Companies now recognize environmental impact and social responsibility in corporate policies.

Regulations and consumer expectations are driving the need to make sustainable practices a part of your business strategy. A common target is the supply chain, which is so critical that the United Nations even published its own [ten principles of supply chain sustainability](#)³. Three of these pillars specifically cover the environment. Supply chain is often the first consideration when a company begins its responsibility program.

Cold chain shipping vehicles primarily use Transport Refrigeration Units (TRUs), a secondary diesel engine that powers the refrigeration. These TRUs are unregulated and highly polluting even in developed countries; they produce 6x as much nitrogen dioxide (NOx) and 29x particulate matter as a modern propulsion engine, and emit up to 50 tons of CO2 [per vehicle per year](#)⁴. On top of the pollution, cold transport also consumes [20% more fuel than room temperature shipping](#)⁵. Cold chain logistics are more damaging to the environment compared to non-cold chain shipping, so reducing or removing cold chain can provide significant benefits.

The packaging used in cold chain shipping is another substantial source of negative environmental impact. Temperature-controlled products are often shipped in expanded polystyrene (EPS) containers (generically referred to as “Styrofoam”). EPS is difficult to recycle and bulky for its weight, resulting in [large landfill buildups](#)⁶. Due to the expansion process used, EPS is 95% air, enabling it to absorb toxins around it and [increase its own toxicity](#)⁷. This is particularly an issue because it escapes into the environment, where it is consumed by wildlife. Not only can this be lethal for the animals that eat the polystyrene, if a human consumes that animal they are at risk as well. It is unsurprising that over 100 cities have [local bans on EPS](#)⁸, yet the shipping industry lags behind. Removing cold chain requirements enables you to ditch Styrofoam for good.

“Lyophilization has many appealing benefits that are hard to ignore. Removing the cold chain reduces costs, simplifies logistics, and promotes environmental responsibility. Now is the time to embrace lyophilization.”

-Cristina Amorim, VP Facilities & EHS and CSO,
Thermo Fisher Scientific

Consumers today look for brands that align with their values. Your customers will not only examine your company's policies, but also those of your partners and suppliers. Selecting a sustainable, environmentally conscious supplier supports your brand. Being a responsible company makes you [more appealing to consumers and to partners](#)⁹.

BROADER APPLICATIONS

Eliminating the need for cold storage through lyophilization increases the applications and scope of your product. One real-world example is vaccines, which have a high rate of waste due to improper storage¹⁰. Many vaccines are sent to developing countries without the ability to correctly store them, increasing waste and reducing medical coverage to these communities.

Lyophilization has been used successfully to [eliminate cold chain requirements in vaccines](#)¹¹, enabling greater field accessibility and use. This concept can be applied to medication, diagnostics, and more.

“Overall, the costs of lyophilization are minimal compared to the savings.”

Lyophilized products are easy to use, maintain functionality, and reduce the need for cold chain by both you and your end user. Argonaut Manufacturing Services has worked with many clients during their transition to lyophilization, each citing their own specific reasons for choosing to go ambient.

“There are a number of compelling reasons why clients pursue lyophilization. The ease of use, stability, elimination of the cold chain, and rapid conversion to the lyophilization process simplify and enhance both processes and profits. Once clients discover the benefits lyophilization offers, they identify multiple opportunities to use lyophilization in their product portfolio, especially in the LyoDose format.”

-Mark Nowakowski, CTO of Argonaut Manufacturing Services,
inventor of LyoDose beads

THE FUTURE OF LYOPHILIZATION

Increased pressure to be environmentally conscious, coupled with cost savings, will continue to drive lyophilization adoption across companies large and small. One obstacle to widespread acceptance is the difficulty of bringing the freeze drying process in-house. The lyophilization field is not currently able to support significant commercial demand, limited by insufficient numbers of expert personnel, expensive equipment, and complex process optimization.

Scientists have taken note of these barriers and moved to address them. The Advanced Lyophilization Technology Hub (LyoHub¹²) was jointly founded by private companies and academic institutions, to support the mission of improving freeze drying science and technology. In order to meet the large-scale demands of the future, the lyophilization field must increase the number of trained users by making the process more user-friendly. The research to enable this, while valuable, is unlikely to be funded by the large government grants that generally support academic investigation. Instead, private companies will need to drive and fund this innovation.

“The lyophilization field is not currently able to support significant commercial demand, limited by: insufficient numbers of expert personnel, expensive equipment, and complex process optimization.”

We can anticipate new technological advances, primarily from lyophilization equipment and service providers, in the coming years. These may include:

Vacuum-foam drying: This is being tested as an [alternative to lyophilization](#)¹³ for biomolecules as it occurs above the freezing point of the solution, but below 100°C. The addition of sucrose can act as a stabilizer and vacuum-foam drying has been tested for stabilization of virus, bovine serum albumin

(BSA), and T-cells. One drawback is that it requires an extremely high vacuum, but we still consider it a promising technology.

Continuous lyophilization: This is a possible variant to routine lyophilization that occurs in batches. This variant has been considered and studied for some time as it may improve consistency of product and add manufacturing flexibility, but it has been difficult to achieve. Recent reports using [spin-drying of vials](#)¹⁴ are encouraging, as are new models.

Increased efficiency: Conventional heat-based lyophilizers have [low energy efficiency of approximately 5%](#)¹⁵, and may require days to process a single batch. Equipment developers will likely deliver improvements in process development, continuous monitoring, and heat transfer leading to increased energy efficiency.

We have previously described the Foundry Model, and believe it is a logical path for lyophilization services as it eliminates expensive barriers that many companies face. In our Foundry Model white paper we discuss that contracting experts for needs, rather than adding in-house capabilities is spreading in the molecular diagnostics industry. Lyophilization requires expert optimization of all parameters at a level above that of a technician, yet these experts are expensive and in short supply. Equipment acquisition can be prohibitively expensive, and the time to market is extended by the need to establish capabilities before production. Working with a contract manufacturer reduces costs and decreases the amount of time spent in development. We predict a rise in specialist contractors of lyophilization services, even with the expected technological improvement in ease of use.

“Working with a contract manufacturer reduces lyophilization costs and decreases the amount of time spent in development.”

With so many benefits and demand already growing, now is the time to introduce the benefits of lyophilization for your product lines. [Contact Argonaut today to get started](#); call us at 1-888-834-8892 or email info@argonautms.com.

CONCLUSION

- Lyophilization reduces costs across a number of points while simplifying logistics.
- Lyophilization positively impacts the environment by reducing pollutants caused by shipping.
- There are fewer user errors using a lyophilized product.
- Product shelf life is often extended if it is lyophilized.
- Obstacles to incorporating lyophilization include expertise, equipment costs, and process development.
- Technology advances in lyophilization will be driven by improvements in efficiency and the need to freeze-dry complex biologics, among other factors.
- Service models provided by contract manufacturing organizations can overcome obstacles to incorporating lyophilization in reagent kits and diagnostics.

¹ <http://pharmaceuticalcommerce.com/cold-chain-focus/biopharma-cold-chain-market-forecast/>

² <https://www.pharmalogisticsiq.com/logistics/articles/cutting-waste-in-the-cold-chain>

³ <https://www.unglobalcompact.org/what-is-gc/our-work/supply-chain>

⁴ <http://cleanleap.com/brace-yourself-cold-chain-coming/environmental-costs-business-usual-cold-chaindevelopment>

⁵ <https://www.pharmalogisticsiq.com/logistics/news/pharma-supply-chain-guide>

⁶ <https://www.bbc.com/news/magazine-33334994>

⁷ <https://www.sierraclub.org/loma-prieta/plastic-bag-and-eps-bans>

⁸ <https://groundswell.org/map-which-cities-have-banned-plastic-foam/>

⁹ <https://www.mckinsey.com/business-functions/sustainability-and-resource-productivity/ourinsights/starting-at-the-source-sustainability-in-supply-chains>

¹⁰ <https://www.the-scientist.com/daily-news/toward-breaking-the-cold-chain-32153>

¹¹ <https://www.ncbi.nlm.nih.gov/pubmed/24382398>

¹² <https://pharmahub.org/groups/lyo>

¹³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3546342/>

¹⁴ <https://www.europeanpharmaceuticalreview.com/article/70823/continuous-controlledpharmaceutical-freeze-drying-technology-unit-doses/>

¹⁵ http://dc.engconfintl.org/biomanufact_iii/70/