Lyophilization and ESG

Reducing carbon emissions (CO2e) of In-Vitro Diagnostic (IVD) assays and reagents using lyophilization

By Wayne Woodard

Overview

We compare predicted CO_2 emissions from a lyophilized molecular IVD assay to a cold chain assay, focusing on transport and storage. Emissions calculations used a publicly available resource with EU EN16258 standard. Transportation examples included truck transport, domestic air, and international air transport. Storage examples included +4°C and -20°C. In all examples, the lyophilized molecular assay had significantly lower CO_2 emissions than the cold chain molecular assay. Organizations considering lyophilizing their molecular assays are likely to see substantial reductions in their CO_2 emissions.

> *"While the lyophilization process is more energy intensive than wet reagent alternatives, the carbon emissions throughout the supply chain of the lyophilized product is clearly advantageous."*
> Cristina Amorim, Sustainability and ESG Professional

Introduction

Reducing the carbon footprint in life science and diagnostic organizations is often a sustainability priority, with net zero carbon dioxide emissions being a long-term goal. Shipping and logistics represent a key opportunity for emissions reduction, as molecular reagents and diagnostic assays utilize cold chain shipping of wet or dry ice, which results in large, heavy shipments. Additionally, reagents and molecular assays are often shipped by air or land, rather than sea or rail, so they require transportation modes with the highest emissions. Finally, cold chain reagents and assays must be refrigerated (+4°C) or frozen (-20°C or -80°C) to retain functionality and stability. Refrigeration is also a major contributor to greenhouse gas (GHG) emissions, with the cooling service industry responsible for over 10% of GHG.[1]

While companies retain control of their facilities and vehicle fleets (scope 1) and purchased electricity (scope 2), they are dwarfed by so-called scope 3 emissions that

[1] https://www.annualreviews.org/doi/10.1146/annurev-environ-012220-034103

include sourcing and shipping.[2] In gaining net zero, scope 3 emissions are some of the most difficult for a life science or diagnostic company to address.

Lyophilization is the process of removing water from a product after it is frozen and placed under a vacuum, allowing the ice to change directly from solid to vapor without passing through a liquid phase. Not only can molecular reagents be lyophilized, but entire molecular assays can also be lyophilized. This can greatly simplify a protocol, making it easier to use for the end-user as the number of pipetting or liquid transfer steps are reduced. With respect to cold chain and logistic emissions though, lyophilization of molecular and IVD assays holds great promise:

- Lyophilized assays can be stable at room temperature, entirely removing cold chain transportation and storage.
- Lyophilized assays weigh significantly less than their aqueous counterparts.
- Lyophilized assays can require smaller packaging, so more assays can be shipped per cubic unit than aqueous assays.
- Lyophilized assays do not require hazardous shipping, compared to aqueous assays that may be shipped on dry ice.
- Lower cost/test in shipping yields more testing for the same spend.

Clearly, lyophilization of molecular assays can impact scope 2-3 emissions but to what extent? In our previous white paper "How to Eliminate Hidden Cold Chain Costs-Lyophilizing Diagnostic Assays" we looked at Total Landed Costs (TLC) of shipping lyophilized assays versus cold chain assays using real world examples and found an 8%-43% TLC savings using lyophilization, dependent on domestic or international shipping (respectively). Here, we will expand the same cases in the previous white paper to now consider the impact(s) on scope 2 and scope 3 emissions.

Background

There are two cases to be examined: a cold chain liquid reagent kit (Case #1) and an ambient stable kit with lyophilized reagents (Case #2). Shipping is evaluated from Carlsbad, CA, 92010 to the following four locations:

- Cambridge/Boston, MA
- South San Francisco, CA
- Raleigh, NC
- London, England

[2] Genomics Firms Tackle Carbon Emissions, Face Obstacles to Net-Zero Goals From Suppliers, Shipping. GenomeWeb Dec 21, 2022 https://www.genomeweb.com/business-news/genomics-firms-tackle-carbon-emissions-face-obstacles-net-zero-goals-suppliers#.ZFU7Ty-B23U

Each shipment is 100 units of a molecular assay that has 8 reactions in each kit. Case #1 represents an assay that is restricted to cold-chain logistics and storage. Case #2 is the same assay that is lyophilized and uses ambient shipping logistics and storage.

Case #1 Cold chain liquid reagent kit

- The kit consists of 2 boxes:
  - Box A ships with gel packs (2°C-8°C) and a volume of 0.21 cu ft
  - Box B ships with a dry ice box (-20°C) and a volume of 0.21 cu ft

Case #2 Ambient stable kit with lyophilized reagents

- The kit consists of 1 box:
  - Lyophilized version of the same kit (above) that ships at ambient temperature with a volume of 0.35 cu ft

As a reminder, Case#1 has two boxes and is a popular design of reagent kits in the molecular diagnostic market. Due to the different storage conditions required by the various reagents, two (or more) boxes are required in a cold chain shipment. Case #2 uses only one box but is slightly larger to accommodate the entire kit: Kits that deploy lyophilization take up less overall shipping volume and typically use only one box because all components are stored and shipped at ambient temperature.

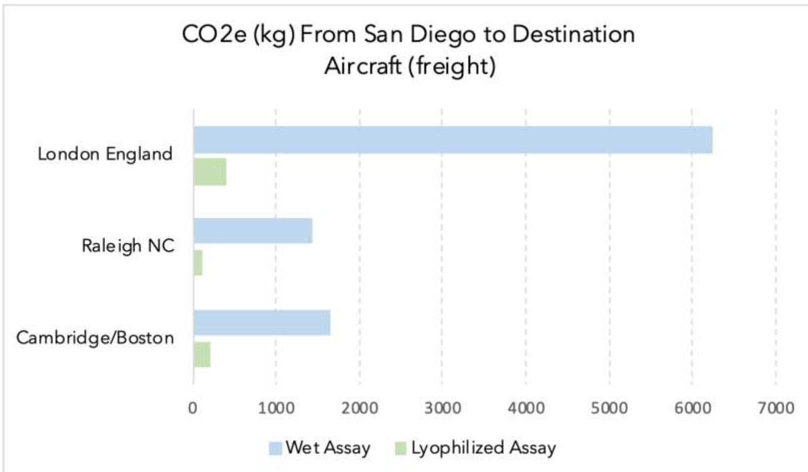
100 units Molecular Diagnostic Assay x 8 reactions

	Lyophilized Reagent Kits		Cold Chain Reagent Kits			
	Domestic Ambient temp.	**International** Ambient temp.	**Domestic** +4C	**Domestic** -20C	**International** +4C	**International** -20C
Packaging dimensions & weights	Load Capacity 2.474 ft^3	Load Capacity 2.474 ft^3	Load Capacity 1.088 ft^3	Load Capacity 0.8466 ft^3	Load Capacity 0.8906 ft^3	Load Capacity 0.7257 ft^3
	7 units @ 0.21 ft^3 8.5 lbs 15 XL Boxes	7 units @ 0.21 ft^3 8.5 lbs 15 XL Boxes	5 units @ 0.21 ft^3 17.5 lbs 20 XL Coolers	4 units @ 0.21 ft^3 25 lbs 25 XL Coolers	4 units @ 0.21 ft^3 29 lbs 25 XL Coolers	4 units @ 0.21 ft^3 34.5 lbs 34 XL Coolers
	15 XL Boxes (ambient) to support Domestic or International shipment of 100 units		45 XL Coolers to support a Domestic shipment of 100 units		59 XL Coolers to support an International shipment of 100 units	
Totals						
Weight of	**Domestic**	**International**	**Domestic**		**International**	
Product	100 lbs	100 lbs	100 lbs		100 lbs	
Shipping Materials	22 lbs	22 lbs	875 lbs		1798 lbs	
Total Shipment	122 lbs	122 lbs	975 lbs		1898 lbs	

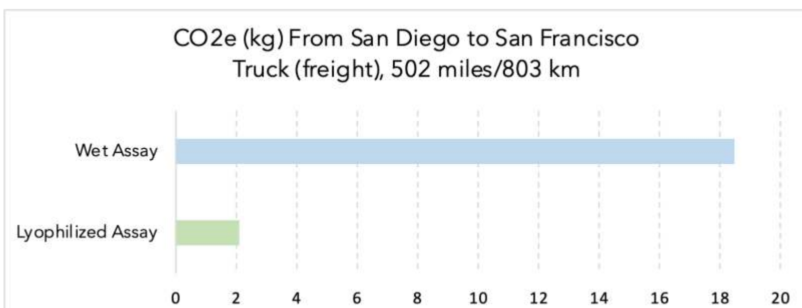
Table 1: Shipping parameters of lyophilized and cold chain kits

Scope 3 Transport Emissions

To calculate scope 3 emissions, domestic transport from Carlsbad, CA to San Francisco, CA will be by road (truck) while all other destinations will be by air (aircraft, freight). The WTW (Well-to-Wheel) emission calculations from CarbonCare.Org[3] are used. WTW includes the production, transportation, and distribution of fuel including the final combustion of energy.



Graph 1: Comparison of CO2e from lyophilized or cold chain assay transported by air, freight.



Graph 2: Comparison of CO2e from lyophilized or cold-chain assay transported by truck, freight.

Air transport has the greatest absolute reduction of emissions, with lyophilization saving 1317 kg (domestic) to 5829 kg (international) CO2e (WTW) in comparison to cold chain assays. This is a reduction of 13.6X to 15.5X in emissions. As air transport emission calculations did not include truck transportation to and from the airport, these emission figures are likely higher. Domestic truck transport emissions of lyophilized molecular assays were reduced by 7.9X to 12.4X compared to cold chain logistic molecular assays with an absolute reduction of 16.3 kg CO2e (WTW).

[3] https://www.carboncare.org/en/co2-emissions-calculator.html. This uses EU EN16258 standard.

For these scope 3 logistics emissions**, lyophilized molecular/IVD assays dramatically reduced domestic transport emissions by 7.9X to 12.4X**, compared to cold chain reagent assays. For **international transport, lyophilized molecular/IVD assays had an even greater emission reduction of 13.6X to 15.5X** compared to cold chain reagent assays.

Scope 2 Storage Emissions

Cold chain logistics require molecular/IVD assays to be stored either refrigerated or frozen. Lyophilized reagents are stored at room temperature. As both types of assays are housed in a facility, likely at ambient conditions, we will not consider differential emissions for the facility space (although a room housing refrigerators and freezers will likely need to be cooled). Instead, we will focus on the extra electrical requirements of the refrigerators and freezers and the subsequent emissions from the electrical production for cold storage, and the emissions required to lyophilize reagents. We will make the following assumptions:

1. Refrigerators and freezers are optimized for full storage. As 100 units in our example cases are below or at the capacity of most scientific refrigerators or freezers, we will calculate only their proportion of use. However, it is realized that freezers or refrigerators are cooled in their entirety: it is not possible to only turn on the portion or shelves that are being utilized.
2. All cooling devices are ENERGY STAR certified.
3. Assays are stored for 3 months.

Refrigeration Type	**Freezer:** UTL -86°C 28 cu ft	**Freezer:** -25°C to -15°C High Performance 29 cu ft	**Refrigerator:** +4°C 21 cu ft
Energy Consumption (kWh/90 Day)	1800 kWh	414 kWh	188 kWh
% Storage Capacity for 100 kits	75%	72%	100%
Total CO2e /90 Day	**499 kg**	**110 kg**	**69.5 kg**

Table 2: Projected CO2e of cold chain storage of assays

For scope 2 emissions, the storage of the cold chain molecular assay kits over a three-month period develops an additional 110 kg of emissions if stored at -20°C compared to the lyophilized molecular assay. If stored at +4°, an additional 69 kg of emissions is created compared to the lyophilized version. In some considerations, this emission rate is optimistic as a) freezers/refrigerators may not be ENERGY STAR compliant and b) freezers and refrigerators generate heat during operations, so the rooms may need to be cooled and c) freezers/refrigerators are rarely used at 100% capacity.

Not all molecular assays can be stored at +4°C or -20°C. The CO2e of products requiring ULT storage is higher. Given the same product sizes, if the assays were to be stored at -80°C, the emissions increase to 499 kg.

Cold storage of non-lyophilized kits produced 179kg-499kg CO2e.

Scope 2 Manufacturing Emissions

Lyophilization requires a different manufacturing process than producing wet reagent assays. The upstream processes are largely identical: thawing and dispensing raw materials. After the master stocks are made, high-volume manufacturing organizations producing wet reagent assays may use robotics to dispense final assay volumes, or may use automated pipettes and dispense by hand. Conversely, there are different lyophilization technologies and platforms. These vary in their capacity, lyophilization times, and energy requirements.

Using the lyophilization manufacturing methods at Argonaut, we calculated the amount of CO2e required to lyophilize reagents, compared to wet manufacturing methods. For the equivalent of 100 kits used in the above example (Table 1), lyophilization required an additional 0.66 kWh, producing 0.244kg CO2e more than using wet reagent production. The lyophilization process also required an additional 4 hours of production time, at an estimated 18.5kg CO2e. Therefore, we estimate the overall lyophilization process developed approximately an additional 18.7kg-36.1kg CO2e compared to production of a wet assay.

After production, wet assays will be stored at +4°C or -20°C, while the lyophilized assays will be stored at room temperature. If we assume the average storage time before shipping is one month, the wet assays develop 23.1kg-36.6kg CO2e due to refrigerated storage, compared to lyophilized assays.

For Scope 2 CO2e, wet reagent and lyophilization assay manufacturing are approximately equivalent. The driving component for CO2e is the amount of time wet assays are stored before shipping. If they can pass QC/QA and all be shipped within four weeks, wet assay manufacturing will likely have lower emissions than lyophilized assays. After four weeks of cold storage, scope 2 emissions for wet assays will be higher than lyophilized assays.

Discussion

In all cases of transport analyzed, lyophilized assays have dramatically lower emissions compared to cold chain logistic assays, reducing emissions by 7.9X (domestic, truck) to 15.5X (international, air).

For a very rough reference, the US performed minimally 1.15B COVID assays as of December 20, 2022.[4] Many COVID molecular assays came from Asia and Europe and with domestic molecular assay developers primarily located on the East and West coasts of the United States, an assumption can be made that the majority of molecular COVID assays and reagents required air transport for delivery. Early in the pandemic, most COVID assays would have been cold chain, while later in the pandemic antigen tests would begin to become prevalent in the US, as over 1B antigen tests were delivered in the US free of charge starting in January 2022. In order to grasp the potential scope of the challenge, and while we could find little public data on this subject, if we assume that a bare majority (51%) of the COVID assays and reagents prior to January 2022 were shipped equivalent in the coast-to-coast model (Carlsbad, CA to Raleigh, NC) and 20% of assays originated overseas, this will result in approximately 3.0B kg of emissions. This is roughly equivalent to the annual emissions of 652K passenger cars in the United States (According to the EPA, the average passenger auto emits 4.6 kg of emissions per year[5]). Lyophilizing the COVID assay format would reduce this by approximately 92% to 52.2K passenger cars. The point is not to determine the amount of emissions resulting from COVID assay logistics, but to better understand the overall potential impact lyophilization of diagnostic assays can bring to reducing emissions. Also, note that the PEW Charitable Trust estimates that approximately 3.3B IVD assays are run in the US every year,[6] a multiple greater than the total number of COVID assays through December 20, 2022.

Further, for storage, lyophilized assays have lower emissions compared to cold chain logistic assays with their requirement for refrigerators and freezers. In our scenarios, lyophilization reduced total CO2e produced during storage compared to cold chain assays. In our example of 100 kits, wet reagent assays developed 179kg-499kg CO2e. This is an emissions reduction greater than 99%.

For scope 2 emissions, manufacturing of wet assays versus lyophilized assays is roughly equivalent if the wet assays are stored less than four weeks. After four weeks of cold-chain storage, wet assay CO2e is greater due to the required refrigeration.

[4] https://www.statista.com/statistics/1028731/covid19-tests-select-countries-worldwide/
[5] https://www.epa.gov/greenvehicles/greenhouse-gas-emissions-typical-passenger-vehicle.
[6] https://www.pewtrusts.org/en/research-and-analysis/reports/2021/10/the-role-of-lab-developed-tests-in-the-in-vitro-diagnostics-market

The balance between scope 2 and scope 3 emissions from lyophilization is interesting. The payoff of lyophilization to reduce emissions for air transport is greater than storage. However, this is reversed for shipping using truck transport as lyophilization emission reductions due to storage is greater than those emitted during truck transport. Depending on the organizational circumstances, some ESG teams may stress the benefits of lyophilization for reducing transport emissions, while others may stress the benefits of reducing emissions by removing cold chain storage. They both can be correct.

Besides not considering short truck transport to and from airports, we also did not cover the “last mile” of transport from storage hubs or depots to final user destination. In both cases, the emission savings due to lyophilization will continue to grow.

Lyophilizing molecular assays can substantially reduce CO_2 emissions, and this will rapidly scale with both the number of assays and the number of shipments. Many organizations will likely find the shipping scale example of 100 kits used in this white paper to be quite low.

Conclusion

This white paper demonstrated the reduction in CO_2 emissions that can be achieved by changing assays from cold chain to lyophilized format. In our prior white paper Total Landed Cost Savings from Lyophilization we covered the significant cost savings that can be gained from lyophilization. Taken together, this is a compelling argument: Lyophilizing molecular assays not only saves money it also helps reduce emissions.

Want to learn more about lyophilization of IVD assays? Visit us at Argonaut Manufacturing Services.