The Environmental Impact of Disposable Technologies

Can disposables reduce your facility's environmental footprint?

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Abstract

We have compared the environmental footprint of a traditional biopharmaceutical manufacturing facility using fixed-in-place stainless-steel equipment, and a facility implementing disposable technologies for cell culture, solution mixing and hold, product hold, and liquid transfer. We accounted for facility size, water consumption, energy use, and carbon emissions from all steps, including even steel manufacture, transporting plastics to and from the facility, plastic incineration, and employees driving to work.

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Introduction to Sustainability

It is becoming increasingly common for individuals and organizations to calculate and publish their environmental footprints, both to understand the impact and to attempt to reduce it. The term *carbon footprint* is now ubiquitous and colloquial. The less common *environmental footprint* extends beyond carbon to include the usage of water and land associated with how individuals live or organizations operate. This paper will address such environmental footprints in the manufacture of standard monoclonal antibodies (MAbs) used as drug therapies.

Traditional facilities with fixed-in-place stainless-steel fermenters, tanks, and associ-

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ated piping and valves are still the prevalent manufacturing methodology to produce biological drug therapies. Many vendors, consultants, and drug companies are endeavoring to replace such traditional facilities with single-use systems to improve flexibility, cost, and also environmental footprint. It may seem paradoxical to claim that a single-use system can have a smaller environmental footprint than a traditional multiuse facility; however, the requirements for sanitization and cleanliness in biological drug manufacture place an extreme environmental burden on the multi-use traditional facility. Sanitization and cleaning is chemical, water, and energy intensive.

Single-use systems do not require such intensive sanitization efforts; their environmental footprints are more a result of their plastic content. Plastics are essentially paraffin-like chemicals with repeating chains of CH_2 molecules. Given this chemical nature, plastics are indeed fuels. The preferred disposal method for such fuels is incineration, with or without energy recapture.

We have analyzed the cradle-to-grave carbon, water, and land footprints, calculated per single batch of a standard MAb, for a traditional fixed-in-place stainless-steel facility and a facility that relies on single-use equipment that is disposed of by simple incineration of all its plastic material. We have included the data from mining the iron ore through the diesel consumed in transporting plastic to the drug manufacturing facility as well as the transportation of waste plastic to the incineration facility, and the incineration of the plastic.

The Rise of Disposable Technologies

We have seen a rapid uptake of disposable technologies in the biopharmaceutical industry. Much of this growth has been in the last five years, although disposables have been around much longer in hospital settings, where they are used extensively. This increasing interest in disposable technologies has naturally been followed by a growing concern about the solid plastic waste generated from their use. This has been an area of interest of the authors who, early in the development and application of disposables, have tried to assess the impact of disposables at the facility level.[1,2]

The disposables-based facility consumes 87% less water than the stainless steel–based facility.

Waste Management Methods for Disposables

The most common methods for disposing of single-use plastics are landfill and incineration, with incineration being more popular. In some cases, incineration can also result in significant energy savings through cogeneration techniques,[3] in which a facility captures the energy generated from burning its waste and uses it to produce heat or electricity.

The possibility of recycling has been assessed by some suppliers, but recycling opportunities are extremely limited, primarily because of the multilayer films of which disposable bag systems are made. Disposable bag films often combine polyethylene, polypropylene, ethylene vinyl acetate, and nylon. It would be more feasible to recycle the silicone tubing that is often attached to bag systems, but that would require segregating tubing and bag, the logistics of which are not simple. In addition, recycling may require pretreatment of biohazardous single-use materials, depending on the process step for which the

Table 1. Key parameters for comparing the environmental impact of disposables-based and stainless steel–based facilities

Parameters	Description
Utility requirements	The model collates all process uses of purified water (PW) and water for injection (WFI) to provide minimum estimates of generator capacities and storage vessel volumes. Steam requirements are calculated from autoclave activities and the sterilization of bioreactors and vessels.
Materials	The materials consist of process media, buffer solutions, and cleaning chemicals (i.e., caustic and acid). The process equipment that requires cleaning includes the stainless-steel bioreactors and preparation or hold vessels.
Consumables	The analysis only accounts for differences in the use of consumables (e.g., bags); it does not include the environmental impact of consumables that are the same in the two processes. In the disposables-based facility, bags are implemented for the cell culture bioreactors and solution preparation and hold operations.
Labor	The labor headcount estimation includes direct production operators, supervisors, quality control and quality assurance staff, and indirect labor. The assumptions include 40 hours per week over 45 work weeks, and 70% availability.
Space	The space requirement for each class (B, C, D, U) is estimated from the equipment in the facility, using a utilization factor of 25%.
Electricity	There are two main uses of electricity: 1) Process electrical loads, which are calculated from the equipment items in the facility; and 2) Electricity used for HVAC equipment, determined from the cfm/kW values for each class.
Steelwork	The amount of steel required for each manufacturing option is determined from the floor area using a typical figure of 180 tons per 1,000 m^2. The stainless-steel equipped facility is a multiple-story building whereas the disposables-based facility consists of one story.

disposable equipment was used. The combination of these factors makes it extremely difficult to develop an economically viable case for recycling disposable technologies in their current configuration. In a recent article, however, Millipore's Director of Sustainability David Newman suggested that homogenous or separable materials (in disposable filters, for example) could increase the feasibility of recycling.[4] The environmental impact of disposables could also be reduced by packaging components in bulk, instead of individually, to decrease the amount of packaging.

Basis of Analysis

Taking into account the current state of disposable technology implementation and the disposal methods described above, we have compared the environmental impact of a commercial MAb process, working with either stainless steel or disposable technologies, looking specifically at the relative environmental footprints of both facilities.

The environmental impact of the traditional stainless steel–equipped and disposables-based facilities has been evaluated using a model based on a commercial MAb process at 3 x 2,000 L scale.[5] The main difference between the two manufacturing options is that one uses stainless-steel equipment and the other implemented disposable bags, tubing, and associated components for:

- cell culture bioreactors
- mixing solutions (buffer and media)
- holding solutions (buffer and media)
- product hold
- liquid transfer tubing and filters.

The stainless-steel equipment requires cleaning after each use. The buffer vessels are cleaned using a simple rinse cycle. The cell culture bioreactors, product, and media vessels are cleaned using a more rigorous cleaning cycle, which includes a purified water (PW) rinse, caustic clean, acid clean, another PW rinse, and a final rinse with water for injection (WFI). Bioreactors and vessels that undergo a full cleaning cycle also require sanitization with steam.

In the disposables-based facility, single-use bag systems are used to prepare and store media, buffers, and products before further processing. The bag systems are provided presterilized, ready for process use, and are not used again; hence, no cleaning operations are required.

In this study, we have focused mainly on the process and the key areas that are affected by choosing disposable equipment, such as facility size, utilities, consumables, and labor requirements. It was not our intention to evaluate materials that are common to both operations. In addition, we have not examined the heating and cooling loads associated with heating, ventilation, and air conditioning (HVAC) systems, instead restricting our HVAC data to the loads needed to run fans. In this way, we eliminated regional factors resulting from climate differences, although this will be to the detriment of the disposables facility. The analysis has not taken into account general cleaning, clothing wash up activities, or the disposal of single-use garments. The single-use plant should have a smaller footprint in these areas because there are fewer employees. The study, therefore, only considers *differences* in the use of consumables (e.g., disposable bags); we did not account for disposables that are assumed to be the same in both facilities. These include small-scale cell culture equipment (e.g., single-use flasks, filters, and pipette tips); filters (e.g., liquid sterile filters, depth filters, UF–DF cartridges); and other common disposable items (e.g., gloves, isopropyl alcohol wipes for cleaning, weigh boats).

Table 1 provides a description of the key comparison parameters. The resulting data sets from the model are then used to evaluate the carbon footprint. The basis for the carbon footprint estimation is summarized in Table 2. The analysis will also take into account differences in carbon emissions that could result from different electricity sources, depending on whether the electricity was generated from: (1) firing coal, (2) firing natural gas in a combined cycle, or (3) the average mix of US sources (coal, gas, hydroelectric, nuclear, other).

Figure 1. Comparison of water usage per batch of antibody in stainless-steel and disposables-based facilities

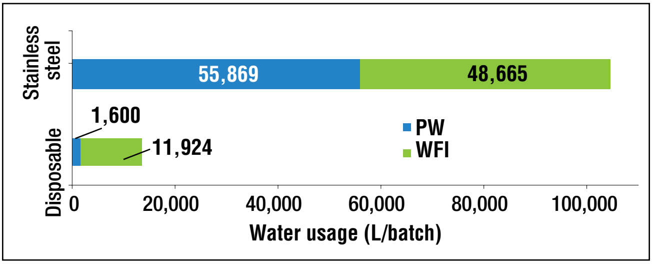


Table 2. Bases for estimating energy consumption and carbon emissions

Item	Energy consumption or carbon emission
Electricity generated by firing coal	1.04 kg CO_2 per kwh
Electricity generated by firing natural gas in a combined cycle	0.39 kg CO_2 per kwh
Electricity generated by average US mix of coal, gas, and other	0.66 kg CO_2 per kwh
Gasoline consumed by workers traveling to work	7.78 L per day*
Water for injection (WFI) production	3 m^3 natural gas per liter of WFI**
Steel manufacture	25 MJ of energy per kg of steel
Steel amortization	Over 15 years (total of 375 batches)
Plastic transportation to and from the biopharmaceutical factory	805 km round trip
Plastic extrusion	0.25 kWh per kg of plastic
Plastic polymerization	0.15 kWh per kg of plastic
Water pumping	75 kW for 6,814 LPM at 80 psig
Energy for air handlers	Estimated from model, unitized per batch

* Daily US gasoline consumption is 1,470.6 million liters. There are 210 million licensed drivers in the US and 90% drive each day.
** The enthalpy (heat content) of steam relative to water at 60 ^{o}F is approximately 3,722 kJ/kg. The boiler is 85% efficient. The energy for chilled water to condense the WFI is 17% of the total energy needed to produce WFI.

Comparing the Environmental Impact

The analysis in this section identifies distinct differences (i.e., in utility requirements, materials, consumables, labor, space, electricity, steelwork, carbon) in the performance of the disposables-based facility when compared to the conventional stainless-steel plant.

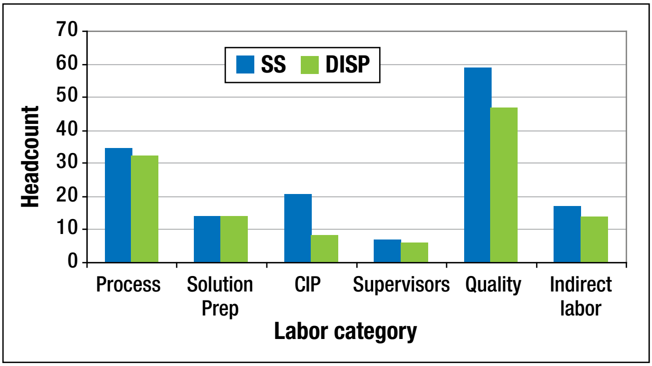
Utility Requirements

Figure 1 illustrates the water usage (PW and WFI) per batch for the two manufacturing options. Implementing disposable bag systems removed the use of stainless-steel bioreactors and product and solution vessels that require cleaning, thus reducing water usage. The model indicates that the disposables-based facility consumes 87% less water than the stainless steel–equipped facility.

Given the reduced water requirements, smaller generators and storage vessels will be needed to operate the disposables-engineered facility. The WFI generator capacity required for the disposables-based facility is approximately 320 L/h, whereas the stainless steel–equipped facility requires a WFI capacity of 1,200 L/h to achieve the same production rate. Using a filling time of 10 h, storage vessels of 12,000 L and 4,000 L are needed in the stainless-steel facility and the disposables-based plant, respectively.

Steam usage results mainly from autoclave activities and the sterilization of bioreactors and vessels. For the stainless steel–equipped facility, a substantial amount of steam (about 880 kg/batch) is needed to run sterilization operations. In the disposables option, the vessels are substituted by single-use bags, thus eliminating the need for clean steam.

Figure 2. Comparison of the labor needed to operate stainless steel–based (SS) and disposables-based (DISP) facilities



Materials

Table 3 summarizes the total amount of process materials and diluted cleaning solutions used per batch. As expected, the quantities used for process media and buffers are the same for both facilities. The single-use setup, however, has eliminated the need for chemicals (i.e., caustics and acids) associated with vessel cleaning operations because the bags are supplied presterilized and ready to use. The model estimates that the quantities of cleaning materials per batch are reduced by more than 95% in the disposables-based facility.

Consumables

The single-use nature of disposable technology has increased the volume of plastic waste. A total of about 880 kg of solid waste per batch is generated. The solid waste is normally incinerated, which may affect air quality, causing environmental concern, and may incur additional manufacturing cost.[2] The exact cost will be linked to the disposal method used and whether pretreatment (decontamination autoclave, or kill with a dose of chlorine dioxide or other deactivator) is required before disposal.

Labor

In the disposable case, because the demand to operate equipment cleaning and sterilization activities is significantly reduced, the labor required to support such tasks decreases. The disposables-engineered facility also may reduce labor requirements in other areas, such as quality. The set-up and turnaround time for disposable systems typically is shorter than for their stainless steel counterparts. All these factors result

Table 3. Comparison of material usage (L/batch) in stainless-steel and disposables-based plants

Category	Material	Stainless steel	Disposable
Process	Media	8,125	8,125
	Buffer solutions	1,998	1,998
Cleaning	Caustic (NaOH)	14,017	450
	Acid (H3PO4)	13,817	250
Total		**37,957**	**10,823**

Table 4. HVAC energy consumption for each class of facility space. The disposables-
and as a result, the total energy consumption for HVAC is 29% lower in that setup.

					Facility footprint (m^2)
Class	ISO	Air changes/h	Activites	cfm/kW	Stainless steel–based
B	7	60	Inoculum; virus removal	1,000	23.04
C	8	30	Downstream purification	1,800	32.16
D	—	20	Cell culture; solution preparation	2,400	273.21
U	—	10	Utilities equipment	3,000	304.45

in a less labor-intensive facility. There is an overall 21% reduction in labor headcount in the disposables-based option compared to the traditional stainless steel–equipped facility. The bulk of the savings in labor headcount is derived from reduced clean-in-place (CIP) activities (Figure 2).

Space

The disposables-engineered facility simplifies hardware installation, design, and storage, leading to more efficient use of space and thus considerably reducing the square footage of the facility. Figure 3 illustrates the facility footprint in square meters for the various

Table 5. Summary of CO_2 emissions per batch for three different electricity sources. The values in stainless-steel facility. Regardless of the energy source, the disposables-based facility reduced

	Coal			Combined cycle natural gas		
Source	SS	DISP	Difference	SS	DISP	Difference
Steam-in-place	0.3	0.0	–0.3	0.3	0.0	–0.3
Clean-in-place	0.9	0.0	–0.9	0.3	0.0	–0.3
Transporting plastic	0.0	0.2	0.1	0.0	0.2	0.1
Pumping water and wastewater	0.0	0.0	0.0	0.0	0.0	0.0
Steel fabrication (amortized per batch)	6.4	3.3	–3.9	6.4	3.3	–4.0
Plastic polymerization (per batch)	0.0	0.9	0.7	0.0	0.3	0.3
Plastic extrusion	0.0	0.6	0.4	0.0	0.2	0.2
Water for injection still	24.7	8.1	–18.7	24.9	8.2	–18.8
Cleanroom energy	0.2	0.1	–0.1	0.1	0.1	0.0
Incinerating plastic	0.0	6.7	5.0	0.0	6.8	5.0
Workers driving to work	67.5	80.1	–7.7	68.0	80.9	–7.7
Total CO_2 per batch	**100.0%**	**100.0%**	**–25.3%**	**100.0%**	**100.0%**	**–25.5%**

Footnote: “SS” indicates a stainless-steel based facility; “DISP” indicates a disposables-based facility.

based facility uses 38% less floor space in Class D and U areas,

	Energy consumption (kWh)		Energy reduction in disposables facility(%)
Disposables-based	Stainless steel–based	Disposables-based	
23.04	19,684	19,684	0
32.16	7,632	7,632	0
130.17	32,420	15,447	23%
204.30	14,451	9,697	6%

area classifications. Table 4 lists the amount of floor space needed in each area classification, based on the types of activities that take place in each. Because the two manufacturing options have the same inoculum preparation and downstream purification sequences, which take place in Class B and C areas, respectively, the floor spaces required for those two classes are the same in both instances. The savings in floor space are obtained from Classes D and U, where the cell culture, solution preparation operations, and utilities equipment are located, with the majority of the space savings coming from Class D. It can be seen that the facilities footprint of the disposables facility is reduced by 243.19 m^2, or 38%, compared to the traditional facility.

the "difference" column are relative to the
CO_2 emissions by more than 25%.

Average US mix of coal, gas, and other		
SS	DISP	Difference
0.3	0.0	-0.3
0.6	0.0	-0.6
0.0	0.2	0.1
0.0	0.0	0.0
6.4	3.3	-4.0
0.0	0.6	0.4
0.0	0.4	0.3
24.8	8.2	-18.7
0.1	0.1	0.0
0.0	6.7	5.0
67.8	80.6	-7.7
100.0%	**100.0%**	**-25.4%**

Electricity

As a result of its smaller facility footprint, the disposables-based facility achieves process electrical savings of about 30%, indicating that such a plant is potentially more energy-efficient. The cubic feet per minute/kilowatt (cfm/kW) values for each class are listed in Table 4. Because the energy required to operate HVAC systems is directly proportional to the floor area, the electricity required to operate classes B and C is the same in the stainless-steel and disposables-based facilities. In the disposables-based facility, however, the total electricity consumed for HVAC operations is reduced by about 29%, which can be attributed to a smaller facility space required in classes D and U.

Figure 4 shows the electrical energy ratios for the two manufacturing options. In the stainless-steel facility, the bulk of the energy is needed to operate Class D, where the cell culture and solution preparation operations take place. When the stainless-steel vessels are replaced with presterilized disposable components, the energy requirement is concentrated in the downstream purification area (i.e., class B) instead of class D.

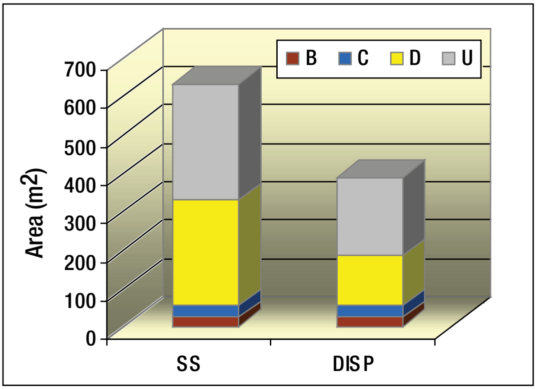
Steelwork

The amount of steel required to build a disposables-based facility is about 62% less than that required for a stainless steel–engineered plant, which can be attributed to the reduced square footage of the disposables-engineered facility and the fact that it is a single-story building.

Carbon

Table 5 summarizes the emission of CO_2 per batch for three electricity sources. In all instances, the emission of CO_2 decreases by about 25.5% for the facility using disposables relative to the traditional stainless steel–equipped facility. The reduction in CO_2 emissions is derived mainly from the reduced usage of WFI, which has more than compensated for the emission of CO_2 associated with the use of plastics (e.g., transportation, polymerization, incineration).

Figure 3. Facility footprint of the stainless steel (SS) and disposables-based (DISP) plants



The benefits of disposables are derived from significant reductions in water usage (87%), space (38%), and energy (30%).

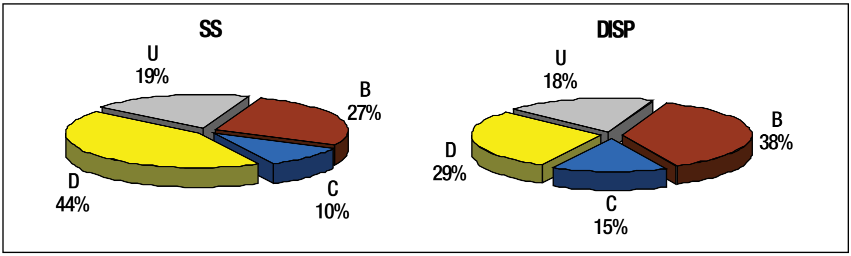
Conclusions

This article has evaluated the environmental impact of the traditional stainless-steel facility and the disposables-engineered plant for the manufacture of a typical monoclonal antibody process at a 3 x 2,000 L scale. The study considers several aspects of the environmental footprint, including carbon output and the usage of water and land. The disposables-based facility reduces the overall environmental impact despite the creation of solid plastic waste. The benefits are derived from significant reductions in water usage (87%), space (38%), and energy (30%) to operate such a facility. As a consequence, there is a substantial decrease in carbon footprint.

In all the fuel source options, the magnitude of the carbon footprint reduction when implementing disposables is about 25.5% when compared to the stainless-steel facility. This is a significant reduction in the impact of manufacturing facilities on climate change. Looking further at the key drivers that give rise to these carbon footprint savings (ignoring all items whose change is less than +/– 1%), the percent reduction attributable to the disposables-based facility is as follows:

- facility size: –4.0%
- water systems: –18.8%
- plastics disposal: +5.0%

Figure 4. The energy ratios for the stainless-steel (SS) and disposables (DISP) options



- number of workers driving to work: –7.7%.

It can be seen that the greatest impact of disposables results from reduced water requirements. For the stainless steel facility, water usage is one of the most significant contributors to the carbon footprint (excluding driving to work). The key consequence of the extensive use of disposables, therefore, is the removal of significant requirements for high quality water by eliminating clean-in-place (CIP) operations. This gives rise to one of the key impacts in terms of reducing the facility's overall carbon footprint: water use.

It is instructive to see that by far the largest contributor to carbon footprint of all categories is workers driving to work. This is significant because disposables lower headcount and therefore reduce carbon footprint by reducing the number of workers driving to work. However, even in the case of the disposables facility, 80% of its carbon footprint is associated with driving to work. This suggests that if we are truly going to reduce the impact of these facilities, we must seek more energy-efficient transportation systems.

This study therefore demonstrates that the use of disposables in biomanufacturing at the 3 x 2,000 L scale actually reduces the impact on the environment when compared to stainless steel. Further developments from single-use suppliers, such as working with recyclable or separable materials and revising current packaging methods for single-use systems, will reduce further environmental impact of disposables.

It should be noted, however, that the overall environmental impact reduction when working with disposables may lessen at larger scale. For example, an evaluation of the usage of water for CIP and the influence of scale indicates that the savings rate is lower for a facility operating at larger scale.[6] ★

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