Life Cycle Assessment of the Prefilled ApiJect Injector

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EXECUTIVE SUMMARY

This study quantifies the environmental impact of five different options for injecting sterile liquid medicines into patients. Specifically, it compares a new, innovative single-dose prefilled injection device and the manufacturing process developed/used by ApiJect Systems, Corp. (collectively referred as the "ApiJect Platform") to four drug dose delivery options long used by the pharmaceutical industry:

1. Single-Dose Glass Vials and Syringes
2. Multi-Dose Glass Vials with Syringes
3. Luer-type Prefilled Syringes
4. Staked-type Prefilled Syringes

All product options were evaluated on the basis of a functional unit of a single 1 mL dose.

This study finds a substantial difference in the environmental impact comparing the ApiJect injection device ("Prefilled ApiJect Injector") and other injection formats, favoring the Prefilled ApiJect Injector across all categories of resource use and environmental impact considered. The differences in global warming impacts are especially noteworthy.

Compared to the Prefilled ApiJect Injector result of 38 g CO_2-eq per dose:

- The estimated Single-Dose Glass Vial impacts are ~125% higher per dose.
- The Luer-type Prefilled Syringe impacts are ~100% higher per dose.
- The Multi-Dose Vial and Staked-type Prefilled Syringe impacts are 65-75% higher per dose.

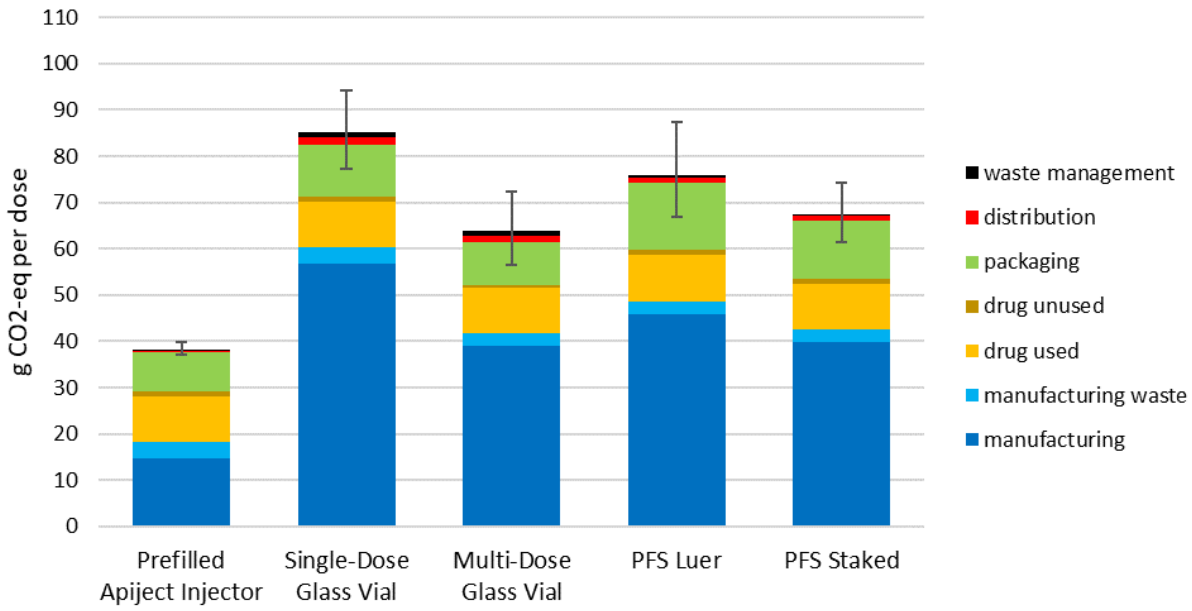

Figure ES1. CO_2e emissions results per 1 mL dose for each drug delivery system, measured in grams of carbon dioxide equivalents (g CO_2-eq). Error bars denote the 90% confidence interval from the Monte Carlo simulations.

The analysis includes comprehensive life cycle stages from cradle-to-grave, encompassing all upstream materials production, manufacturing, inspection, packaging, transportation, use and waste management. The report is based on data from materials quantities and energy inputs collected from the manufacturing operations utilized for the Prefilled ApiJect Injectors. For the four other options, materials quantities are weighed from samples, while process parameters are estimated from values in the literature and expert interviews. The report applies internationally standardized (ISO 14040 and 14044) methods of Life Cycle Assessment (LCA) to compare environmental impacts of the Prefilled ApiJect Injector and the four product alternatives.

This study uses several alternate modeling scenarios to test the robustness of the results to various process, location, and transportation assumptions. In all modeling scenarios, the order of environmental preference stays the same, with the Prefilled ApiJect Injector results being consistently the lowest among the options considered.

The importance of this study's findings is tied to an increasing recognition that health care and its supply chains are important contributors to greenhouse gas emissions (GHG). Today, they collectively represent 8.5% of U.S. GHG emissions, and approximately 5% of global emissions. A recent UNITAID study of 10 critical lifesaving products found that these 10 items alone contribute 3.5 million tons of carbon dioxide equivalents of GHG emissions, approximately equal to the entire national emissions of Iceland.[1]

The Prefilled ApiJect Injector uses a polymer resin container filled with a sterile liquid dose that is created and sealed in a continuous process. By attaching a needle hub to the drug container, a new type of single dose prefilled injector is formed. Among its many benefits, including high-speed, high efficiency manufacturing and a simplified supply chain, the Prefilled ApiJect Injector is designed to improve product safety by preventing microbial contamination risks associated with multiple withdrawals from a vial.

In addition to its lower global warming results, the Prefilled ApiJect Injector makes less use of water than the other options evaluated. A typical single-dose glass vial requires 750 mL of direct water for cleaning and sterilization for a single 1mL dose. In contrast, the Prefilled ApiJect Injector requires approximately 6.4 mL of water for the manufacturing process.

ABBREVIATIONS AND NOTATION

Al	Aluminum
AlO	Alumina
API	Active Pharmaceutical Ingredient
BFS	Blow-Fill-Seal
CA-QC	Canada – Quebec
CCIT	Container Closure Integrity Testing
CO_2-eq	Carbon Dioxide Equivalents
DI	Deionized (water)
DQI	Data quality indicator
eGRID	Emissions & Generation Resource Integrated Database
EO	Ethylene Oxide
FDA	Food & Drug Administration
g	grams (of mass)
GHG	Greenhouse Gas
GLO	Global average life cycle inventory dataset
GWP	Global Warming Potential
HDPE	High-Density Polyethylene
IPCC	Intergovernmental Panel on Climate Change
ISO	International Organization for Standardization
kg	kilograms (of mass)
kg-km	kilogram-kilometers (of freight)
kJ	kilojoule (of energy)
km	kilometers (of distance)
kW	kilowatt (of electrical power)
kWh	kilowatt-hour (of electrical energy)
L	liters (of volume)
LCA	Life Cycle Assessment
LCI	Life Cycle Inventory

LCIA	Life Cycle Impact Assessment
LDPE	Low-Density Polyethylene
mL	milliliter (of volume)
MJ	megajoule (of energy)
p	Power factor parameter used in scale-up calculations
PE	Polyethylene
PET	Polyethylene terephthalate
PFS	Prefilled Syringe
PP	Polypropylene
PVC	Poly(vinyl chloride)
RoW	Rest-of-World average life cycle inventory dataset
SRVC	Southeast Region - Virginia Carolina (electricity grid sub-region)
TRACI	Tool for Reduction and Assessment of Chemical and other Environmental Impacts
USEPA	United States Environmental Protection Agency
UV	Ultraviolet
V	Internal volume parameter used in scale-up calculations
VI	Visual Inspection
Wh	watt-hour (of electrical energy)
WHO	World Health Organization

1. INTRODUCTION

This report contains the results of a study that compares the environmental performance of several options for injecting sterile liquid medicines into patients, in terms of their contribution of greater greenhouse gas emissions and several other categories of environmental impact. The studied options include four traditional methods and one new option from an early-stage medical technology company, called ApiJect Systems, Corp. (ApiJect). The Prefilled ApiJect Injector comprises a proprietary prefilled plastic device for injecting humans or animals with a single dose of a sterile liquid. The company claims its manufacturing process and materials reduce life cycle greenhouse gas (GHG) emissions (*i.e.*, carbon footprint) and other environmental impacts, relative to those impacts associated with four product alternatives: single and multi-dose glass vials combined with disposable intramuscular syringes and needles as well as luer- and staked-type prefilled glass syringes. We do not make comparisons with "autoinjectors," cartridge-based systems, or vial adapters in the evaluation, because those product presentations are not directly comparable to the ApiJect Platform and its target market.

There is increasing recognition that health care and its supply chain are important contributors to GHG emissions, representing 8.5% of US national GHG emissions[2] and approximately 5% of global[3]. In response, 84 countries and counting have signed onto the WHO Alliance for Action on Climate Change and Health framework with decarbonization targets for their health care sectors. The majority of health care sector GHG emissions are due to their supply chains, so one focus of national decarbonization efforts is to gather information about the carbon footprint of medical devices and supplies, including drugs. A recent UNITAID study of 10 critical lifesaving products found that they contribute 3.5 million tons of carbon dioxide equivalents of GHG emissions, approximately equal to the entire national emissions of Iceland.

This report applies internationally standardized (ISO 14040 and 14044)[4] methods of Life Cycle Assessment (LCA) to compare environmental impacts of the four product alternatives and the ApiJect system. LCA is a quantitative environmental assessment approach that has been applied widely to evaluate and compare products and processes. LCA comprehensively considers emissions and impacts that occur over a product's life cycle, typically including the stages of extraction of raw materials and product manufacturing, transportation, use, and waste management. In LCA, product options are compared on the basis of their function, so that product options with different physical forms and compositions but equivalent performance can be compared fairly. LCA evaluates product options along multiple dimensions of environmental impact (*e.g.*, global warming, toxicity, water use) using consensus science models that link emissions to environmental changes, harmful exposures, and impacts to human and ecosystem health.

2. THE APIJECT PLATFORM

2.1. Background and Design

Blow-fill-seal (BFS) refers to a globally used aseptic fill-finish process where a polymer resin container is formed, filled with a sterile liquid dose and sealed, all in a continuous process. Ophthalmic products and respiratory therapies are the most common pharmaceutical applications of BFS technology, but BFS can be used for a wide range of other sterile liquids including small molecules, biologics, and vaccines. ApiJect is seeking to further expand the pharmaceutical uses of BFS to include injectable drugs by incorporating an attachable needle into its platform of different drug containers. The Prefilled ApiJect Injector is a device for administering a single dose of a sterile liquid into humans and animals, by attaching a proprietary hard-plastic needle hub (labeled part 1) to a BFS container (labeled part 2). This Prefilled ApiJect Injector forms a new type of single dose prefilled injector, using a design and manufacturing processes that produce BFS container and the attachable plastic components (Figure 1).

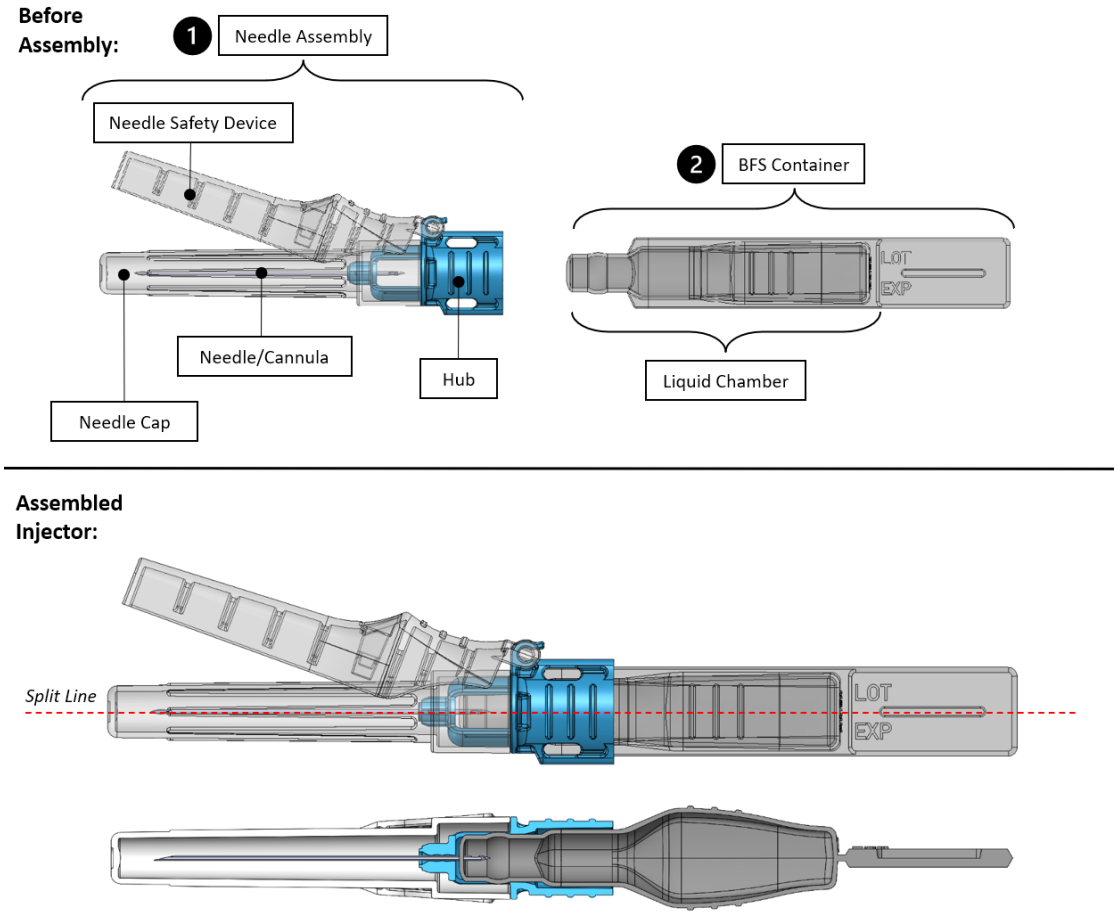

Figure 1. Reference Image of an example of a Prefilled ApiJect Injector design (Note: Prefilled ApiJect Injector and Needle Hub have not been cleared by regulators).

The Prefilled ApiJect Injector is designed to provide a prefilled, ready to use presentation that prevents dose accuracy issues (*e.g.*, measurement, dilution, or dead space) associated with use of drug products in vials. Also, the Prefilled ApiJect Injector is designed to improve product safety by avoiding microbial contamination risks associated with multiple withdrawals from a vial. Additional benefits associated with the prefilled presentation of the durable plastic BFS Container, and the BFS manufacturing process, include reliable dose delivery, product integrity, low breakage rates, and manufacturing and supply chain efficiency. The Prefilled ApiJect Injector is user-assembled at the point of care by a healthcare professional or other user, who first attaches the needle hub to the distal end of the BFS container. In some designs, the connector-to-BFS attachment is maintained by an interference fit between attachment features integrated into the BFS container and the needle hub designs. During the assembly process, the proximal end of the needle pierces the filled BFS container to access the drug product, activating the fluid path. To deliver the drug, the needle cover is removed, the needle is inserted to the appropriate target tissue and depth, and the BFS container is squeezed between the thumb and index finger to fully deliver the dose. The needle is then withdrawn, and the needle safety device is manually engaged, shielding the needle. The entire Prefilled ApiJect Injector is then placed in an approved sharps container for disposal.

2.2. Manufacturing Process Description

The manufacturing operation for the BFS container uses conventional BFS equipment and processes consistent with practices outlined in FDA guidance: Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice (2004), and its Appendix 2 - Blow-Fill-Seal Technology. Figure 2 shows a process flow map of the manufacturing process.

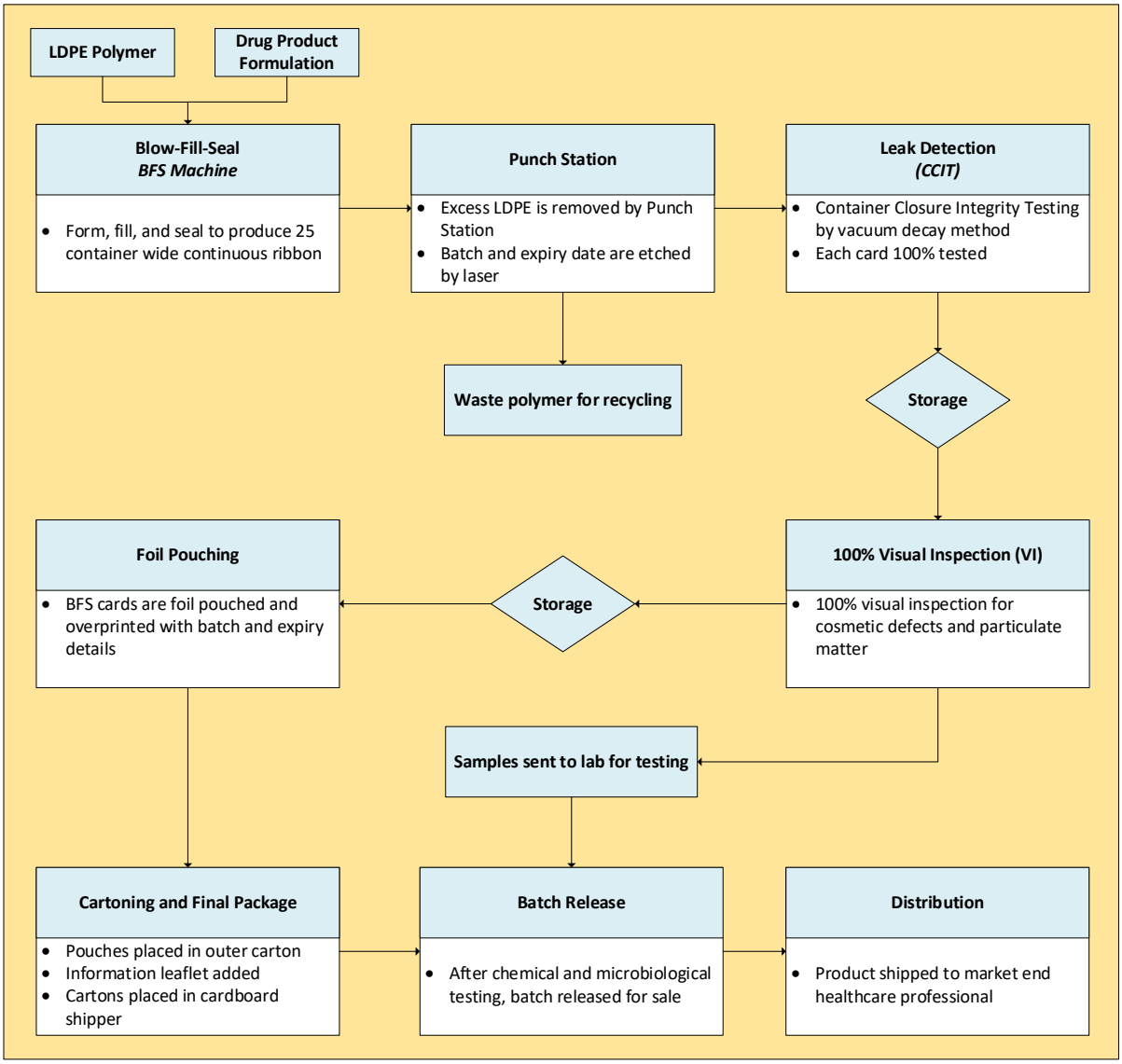

Figure 2. BFS Manufacturing Process Flow Map.

The BFS container manufacturing process takes place in a cleanroom environment meeting Class 10,000 (ISO 7) requirements. It is an automated process in which containers are thermoformed from LDPE resin, filled with the liquid drug dose, and then sealed in one continuous operation. The LDPE is extruded (extruder head temperature is ~165-210°C) around the fill needles in a tubular form and the BFS machine inflates the tube of extruded molten LDPE resin with sterile air and vacuum pulls the resin into mold cavities. The fill needles then aseptically fill the primary containers with the drug dose and then the head molds come together to seal the containers,

forming a ribbon of 25 BFS containers (Figure 3). The continuous ribbon of 25 container sets is then discharged from the BFS machine.

In order to utilize BFS for filling of temperature-sensitive drugs (as many injectable drugs are), heat in the system is mitigated through proprietary cooling methods throughout the BFS process. Cooling takes place within the container formation and filling process as well as immediately after forming; whereby, containers are rapidly cooled using chilled air.

Figure 3. BFS ribbon discharge of BFS machine entering punching station

The ribbon enters the punch tooling where the lot number and expiry date are laser engraved on each BFS container. Also, the punch tooling cuts the excess LDPE plastic away from the 25-container set and sends it down a conveyor. This container set then enters a separator, where it is split into five cards of five connected BFS containers each. These five cards of BFS containers are then sent through in-process inspection, including leak detection and visual inspection. They are then packaged in foil pouches that are inserted into shelf cartons along with paper inserts, grouped into corrugated cardboard shippers, stacked on standard wooden pallets, wrapped, and shipped.

The BFS containers are cross-labelled for use with needle hub assemblies. The manufacturing operation for the needle hub makes use of conventional injection molding and needle forming. The connector/hub, needle safety device, and needle cap are manufactured via injection molding of medical grade polypropylene. The double-ended needle is cannula formed from a stainless-steel tube. Once formed, the cannula is fixed into the connector/hub using UV adhesive. The needle cap and needle safety device are fitted onto the connected needle and connector to form the needle connector assembly. The needle hub assembly is then packaged into a soft pack and sterilized via ethylene oxide sterilization. The needle hub assemblies are bulk packaged for distribution to ApiJect.

3. CONVENTIONAL DRUG DELIVERY SYSTEMS FOR COMPARISON

3.1. Glass Vials

Glass vial filling is the most common fill-finish process for sterile liquid pharmaceuticals. In this fill-finish process, a glass vial is sterilized, filled with a specific amount of sterile liquid, and then sealed with a rubber septum, plastic cap, and aluminum crimp. During drug administration, a plastic syringe with an attached needle is used to withdraw the sterile liquid from the glass vial. Once the dose is in the syringe, the dose prep needle is disposed, and a clean administration needle is attached to administer the liquid through intramuscular injection. Vials can be single-dose or multi-dose. Figure 4 contains reference images of typical vial components.

a) Vial, rubber septum, and crimp cap.

b) Dosing syringe.

c) Dose Preparation Needle.

d) Administration needle with needle safety device.

Figure 4. Reference images of vial components: a) vial, rubber septum, and crimp cap; b) dosing syringe; c) dose preparation needle; and d) administration needle with needle safety device.

3.2. Prefilled Syringes

Prefilled syringes are another established system for drug packaging and delivery, wherein glass barrels (staked or luer type) are siliconized, sterilized, filled with a specific amount of sterile liquid, and capped at one end with a plunger attached to the other. For luer type prefilled syringes, a needle assembly must be attached to administer the dose. Figure 5 contains reference images of both the staked and luer prefilled syringe types.

Figure 5. Reference image of prefilled syringe presentations: luer type with separate needle (top) and staked (bottom).

3.3. Medical Glass Production and Fill-Finish

Glass vials and prefilled syringe barrels are typically produced from high-purity borosilicate glass. Sand and additives are melted in a furnace above 1500°C and drawn out into long canes of varying diameters. Glass canes are then cut and formed into individual glass vials or syringe barrels, which are cooled, blown with dry air, and checked for shape. The glass pieces are then annealed at ~565°C to alleviate material stresses in the glass. Glass is then shipped to the fill-finish station where it is inspected, washed with deionized water or water for injection, depyrogenated, filled, and sterilized. Glass vials, needles, and prefilled syringes are packaged similarly to the ApiJect Platform in shelf cartons and grouped into corrugated cardboard shippers.

4. PRIOR LIFE CYCLE ASSESSMENT STUDIES OF DRUG PACKAGING

Past research has compared the processes and environmental impacts associated with different forms of liquid drug packaging.

An early study by Belboom *et al*. (2011)[5] conducted by researchers at the University of Liège compared glass vials to polymer vials produced by Aseptic Technologies (Gembloux, Belgium). The study was cradle-to-grave, meaning that it considered all stages of the product life cycle from material production, manufacturing of the vials, fill-finish, transportation, use, and end-of-life disposal. The two vials were of comparable size (1 mL), but the polymer vials were radiation sterilized before arriving at the fill-finish process and filled via needle through a cork and recapped, while the glass vials had to be cleaned and steam sterilized immediately prior to filling. The glass vial required more than five times the mass of materials of the polymer vial, which proportionally increased energy use and emissions associated with glass manufacturing. At end-of-life, both vials were assumed to be incinerated, but only plastic has calorific value and releases emissions. Energy from plastic combustion was assumed to generate electricity (the norm for European incinerators) and so was assigned a credit, whereas glass was assigned zero credit. This study found that, over the entire life cycle of both packaging options, the polymer vial system had a 23% lower carbon footprint than the glass vial system, primarily due to a lighter product weight and the avoidance of sterilization steps during fill-finish.

A related study by Dhaliwal *et al*. (2014)[6], conducted by the LCA consultancy Earthshift in collaboration with GE Healthcare, also evaluated polymer versus glass bottles but for the storage of contrast agents rather than pharmaceuticals. Again, the sizes were comparable (100 mL) and delivered an equivalent amount of liquid. The polymeric vial was a GE Healthcare product called +*PLUS*PAK™, comprised of pharmaceutical-grade polypropylene. In this case there was no difference in the filling process, and similar assumptions to Belboom *et al*. were made around end-of-life incineration of plastic and glass. This study found an even greater difference in GHG emissions between the two packaging types, with the plastic bottle having 55% lower life cycle emissions than the glass bottle, the biggest differences being from material manufacturing.

More recent work by Bassani *et al*. (2022)[7] set out to compare all major drug packaging types used in Europe for solid drug tablets, including HDPE plastic and glass bottles and all associated secondary packaging. As in prior studies, the glass bottles were much heavier, by a factor of ~4 but the work focused on materials and did not consider differences in cleaning or sterilization. Even so, this study found approximately 10% lower GHG emissions for plastic bottles.

Other environmental research has been motivated by the large carbon footprint of pharmaceuticals in the context of system-wide or national healthcare greenhouse gas emissions[8], as well as the low manufacturing volumes and global scarcity of some medications. Innovations in drug packaging and delivery may reduce drug wastage and alleviate environmental and supply chain pressures. Prior research has identified prefilled syringes as having significant potential to reduce drug wastage compared to glass vials.[9]

Industry has also commissioned life cycle assessment or carbon footprint studies for specific products, especially those that have been designed with sustainability goals in mind.

5. LIFE CYCLE ASSESSMENT METHODS

This study uses the ISO standard for LCA (14040), which defines four standard phases to any analysis: (1) Goal and Scope (2); Life Cycle Inventory Analysis; (3) Life Cycle Impact Assessment; and (4) Interpretation.

5.1. Goal and Scope

5.1.1. Goal

The goal of this study was to quantify the potential environmental impact of five injectable drug delivery options, compare the results to determine if there was a statistically significant difference in the potential environmental impacts of the options, and identify key drivers of sustainability and opportunities for planning future production designs, configurations, and locations.

The project was commissioned by ApiJect Systems, Corp., and conducted by environmental engineer and LCA practitioner Dr. Matthew Eckelman and economist Dr. Robert Litan, with support from the engineering and subject matter experts at Kymanox Corporation. The results of this study will be used to inform design and production decisions at ApiJect, and support marketing claims about the environmental profile of the product. This study contains comparative assertions intended to be disclosed to the public. The target audiences for the report are internal product developers (for process improvement) and health care system stakeholders including administrators, clinicians, procurement specialists, and sustainability professionals.

5.1.2. Product Systems

This LCA considered five product alternatives:

- Prefilled ApiJect Injector
- Single-dose glass vial with plastic syringe and two hypodermic needles for drug drawing and drug administration
- Multi-dose glass vial with (per dose) plastic syringe and two hypodermic needles for drug drawing and drug administration
- Glass prefilled syringe with luer needle assembly
- Glass prefilled syringe with staked needle assembly

5.1.3. Functional Unit and Reference Flow

We evaluated the above alternatives based on the delivery of a single dose of 1 mL of drug, which is set as the functional unit of comparison for the study. The reference flows are the Prefilled ApiJect Injector, the single-dose glass vial, the prefilled syringe (luer and staked), which are all designed to deliver 1 mL of drug. The multi-use glass vial has a usable volume of 10 mL, and its inventory results are scaled according to the number of 1 mL doses that it can provide. Other functional considerations such as shelf-life, durability during transit, ease of use, and clinical efficacy were assumed to be equivalent based on design specifications and expert judgement and were not separately considered in the analysis.

5.1.4. System Boundary

The system boundary of the analysis was cradle-to-grave, encompassing all upstream materials production, manufacturing, fill-finish, inspection, packaging, transportation, use, and end-of-life waste management. Drug administration (use stage) was assumed to be equivalent among all options. Because some product options have inherently higher drug wastage than others and this difference is material to the environmental performance of the different drug delivery options, the scope included the production and filling with a generic drug, chosen here as a representative data set from Parvatker *et al*. (2019).[10] Inputs related to production of machinery, infrastructure, general building operations, and personnel were excluded consistently across product options, which is a common set of scope assumptions in life cycle assessment of manufactured products. Figure 6 shows the system boundary for the ApiJect, glass vial, and pre-filled syringe options with flows labelled according to data source.

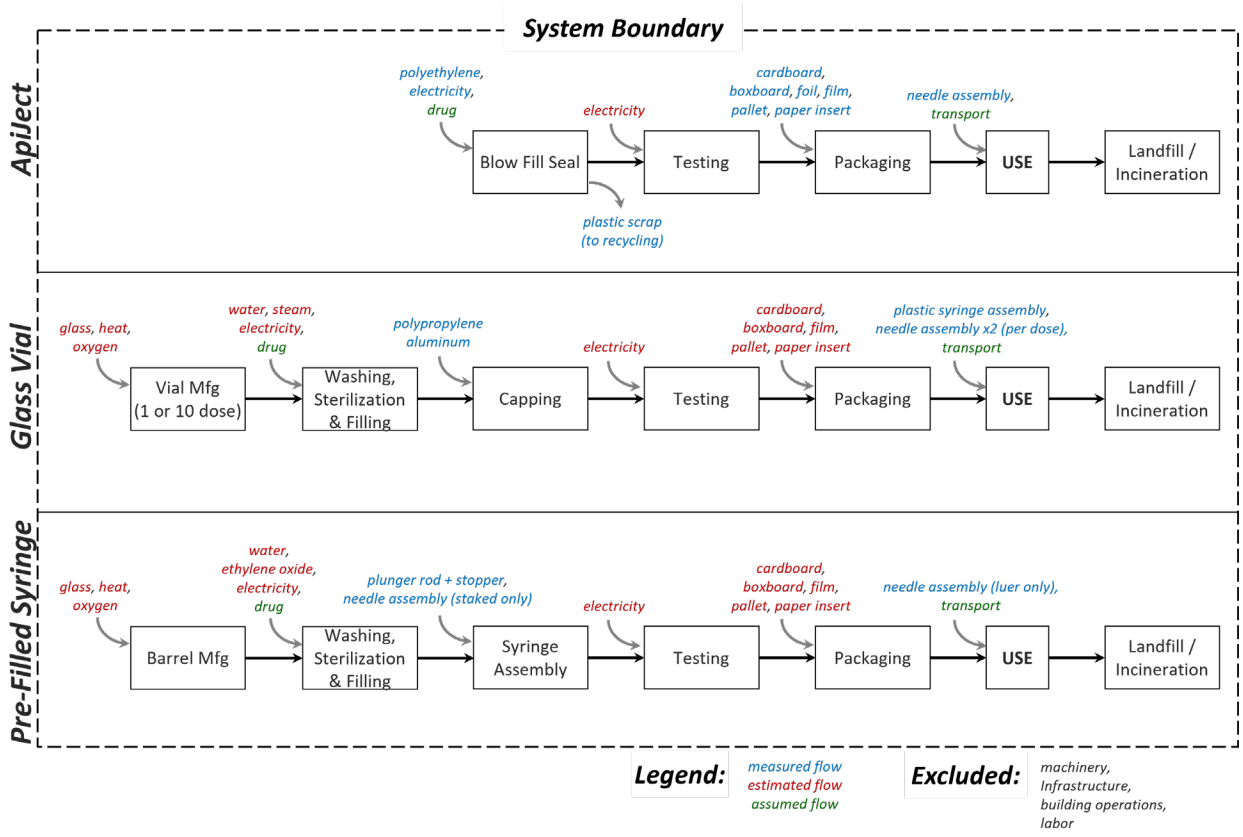

Figure 6. System boundary diagram.

5.1.5. Data Sources and Modeling Procedures

Life cycle assessment modeling was performed with the LCA software openLCA v2.0.1 (Berlin, Germany). Data sources for quantities and physical modeling parameters for materials and energy were directly from manufacturers via site visits, deconstruction and weighing of samples, or surveys of the literature. All input data were validated through external expert interviews arranged by Kymanox.

Each measured or modeled input of materials and energy was linked to a life cycle inventory dataset that describes its supply chain emissions all the way back to raw material extraction. This study prefers data from the widely used commercial database ecoinvent v3.10 (Dübendorf, Switzerland). The cut-off system model was used, meaning that all burdens are assigned to the first product and that no credits are assigned to recycled materials; rather recycled materials are provided burden-free to the next product life cycle. As drug packaging in the U.S. is typically 100% virgin primary material, there are no credits for recycled content provided.

There are no co-products in any of the product systems considered, so allocation was not applied in the foreground system. Economic allocation is the default allocation method for the ecoinvent v3 database for all background datasets. The LCA used an attributional approach.

The analysis included all operational material and energy flows. No universal cut-off thresholds were applied.

5.1.6. Data Requirements, Data Quality Requirements, and Data Quality Assessment

Data requirements are set for temporal, geographic, and technological considerations. For temporal considerations, the study is primarily based on measured data from 2023, with other values and parameters taken from relevant professional publications in the past five years. We use older publications only in cases where recent reports were not available. Subject matter experts have confirmed that the data and conclusions of the peer-reviewed studies that were used for secondary data are still valid.

For geographic considerations, the analysis uses a production location for ApiJect in the Southeastern USA, where test runs are currently being carried out, while the ApiJect needle/connector is produced in Southeast Asia. Supply chains for medical packaging are global, with major suppliers in France, Hungary, UK, US, Mexico, Germany, Switzerland, and Japan. Given the range of potential upstream production locations, we gave preference to global average (GLO) datasets, followed by rest-of-world (RoW) datasets. Measured data for the Prefilled ApiJect Injector were taken from the actual equipment that will be used in production.

For technological considerations, for upstream suppliers and for the other drug packaging and delivery options, the LCA project team selected datasets and modeling assumptions that matched the dominant technology in the marketplace (>50% market share). In cases where no data were available for the technology type or scale, we applied well-documented adjustment factors, as noted in the LCI Analysis section. Foreground data for the Prefilled ApiJect Injector system were collected directly and reflected the exact equipment and technology processes used in production.

We assessed data quality by using the Pedigree matrix approach of Weidema and Wesnæs (1996),[11] which is the same matrix to quantify data uncertainty as in the ecoinvent database, the main

background database that was used in this study. More specifically, we assessed data quality according to five indicators:

- reliability
- completeness
- temporal correlation
- geographic correlation
- technological correlation

Data quality indicators were included for all foreground data by assigning a score between one and five for each of the indicators, one being the highest quality and five the lowest. Pedigree matrix values are used to determine a geometric standard deviation for each point value estimate in the foreground data, which then defines a probability distribution function for each model parameter. The default probability distribution used by the ecoinvent database is the log-normal distribution, which we used also for all foreground data. Monte Carlo simulation was then sampled from each model parameter's probability distributions during the uncertainty analysis to create confidence intervals for each set of results. Full tables for the Data Quality Analysis are provided in Appendix C.

Additional data quality considerations included:

- precision, whereby 3-4 significant figures were used for all modeling parameters, and all modeling parameters were assigned a measure of variance derived from the Pedigree Matrix approach described above;
- consistency, whereby inventory assumptions (regarding materials, distances, end-of-life disposition, etc.), modeling procedures, data and data quality requirements, and LCIA methods were applied in the same manner to all product options, and a single LCI database was used for all modeling;
- reproducibility, whereby full inventory and impact assessment numerical tables are provided;
- data sources, as described in Section 5.1.5 – Data Sources and Modeling Procedures; and
- uncertainty, as described in Section 5.4 – Interpretation.

5.1.7. Critical Review

The results of the LCA study are intended to support external communication. Therefore, to conform to ISO 14044, a critical review of the study was conducted. Since it is a comparative study, the review is conducted by an independent review panel. The members of this review panel were:

- Terrie Boguski, Harmony Environmental (panel chair)
- Cassandra Thiel, New York University
- C. Jason Pierce, LCA Consultant and Certified Practitioner

The review panel was provided with a copy of the LCA study and responded with comments regarding adherence to the ISO LCA standards as well as general questions and suggestions. Study authors responded to each reviewer's comment and made appropriate revisions to the study. A copy of the review panel report and responses can be found in Appendix D.

5.2. Life Cycle Inventory Analysis

Data for the ApiJect system were all measured directly. Data for the alternative product systems were measured directly for product and packaging materials and derived from literature sources for manufacturing processes and flows, as noted below. Data was obtained for all flows (there was no missing foreground data). Complete tables of foreground data quantities, processes, product specifications, and background data sets are provided in Appendix B, Tables B1-B5.

Electricity was assumed in all cases to be medium-voltage in the appropriate market: the Southeastern Electric Reliability Council (SERC) region for ApiJect BFS container manufacturing in the United States, the Korean national grid for ApiJect needle assembly in Korea, and the global average electricity generation for all other electricity flows where the location of production was unknown. In order to control possible bias from knowing the location for some processes but not others, a scenario was run utilizing global averages for all electricity flows (see Section 6.4).

Energy use data for the Prefilled ApiJect Injector were estimated using the metered power usage for the BFS machine measured on-site and using the rated power of the single-phase chiller and optical inspection equipment as listed on their nameplates. Actual power usage for the chiller and optical inspection equipment will be lower than the rated power, so this represents a conservative assumption. Power usage for each piece of equipment was combined with the measured throughput of 29,032 vials per hour to arrive at the energy use per vial, as shown in Table 1.

Table 1. Equipment used in Prefilled ApiJect Injector manufacturing.

Equipment name	**Power Rating** [kW]	**Energy per unit** [Wh/unit]
Blow-Fill-Seal Machine	84.0	2.89
Chiller	14.4	0.49
Optical Inspection	21.6	0.74

Energy use data for glass vial manufacturing were derived from Belboom *et al*. (2011), who found resource consumption rates of 1.27 kg oxygen and 52 MJ of natural gas-derived heat per 4.48 kg of glass vials. These values are scaled linearly to the single-dose, multi-dose, and glass syringe manufacturing processes. Deionized water used for washing the vials is assumed to be 10% of the vial volume based on expert judgement.

Sterilization is required for multiple components of the glass vials and prefilled syringe options. Based on interviews with a Kymanox subject matter expert and literature review, we determined that the most representative scenario is that glass vials, vial stoppers, and syringe plungers are steam sterilized, while the glass syringes are sterilized with ethylene oxide (EO). A typical sterilization run for low-volume/high-value products is 12,000 units per batch sterilized in a 400 L sterilizer.

It was not possible to collect inventory data directly from sterilization equipment used for contemporary vial manufacturing. Instead, we used values from literature for a smaller unit with an internal volume of 54 L from Adler *et al*. (1998)[12] who compare EO, plasma, formaldehyde, and steam sterilization. These values were scaled up to the larger 400 L unit using a typical cost scale-up factor for chemical equipment[13] of 0.7 to derive a scale-up factor for the power usage P_i of the 400 L unit as compared to power usage P_0 of the 54 L unit from Adler *et al*.:

$$\left(\frac{P_i}{P_0}\right) = \left(\frac{V_i}{V_0}\right)^p = \left(\frac{400}{54}\right)^{0.7} = 4.06$$

Assuming the 12,000-unit capacity applies to all vials, stoppers, and syringes, Table 2 shows the quantities of steam, water, and EO used for the two types of sterilization.

Table 2. Resource requirements for sterilization

Equipment name	**Steam @ 54 L** (Adler *et al.*, per batch)	**Steam @ 400 L** (this study, per dose)	**EO @ 54 L** (Adler *et al.*, per batch)	**EO @ 400 L** (this study, per dose)
Heat	3.8 kWh	0.0013 kWh	43.5 kWh	0.015 kWh
Deionized water	1100 L	0.372 L	200 L	0.068 L
Ethylene oxide	-	-	3 kg	0.001 kg

Wastage rates at different manufacturing steps in the ApiJect Platform were determined from actual production data and operator interviews. This includes wastage rates for the portion of the polyethylene panel that is punched out and recycled for downstream plastic applications, as well as rejected product following vacuum leak testing results and visual inspection. Rejection rates for glass vials and prefilled syringe options are set at 5% based on Belboom et al. (2011).

Prefilled ApiJect Injector and prefilled syringe options all contain 1.1 mL of drug, of which 1 mL is administered and the remainder is assumed to be discarded after use, and so a single unit is used for comparison in this LCA. The single-use glass vial option contains 1.1 mL of drug, of which 1 mL is administered and the remainder is assumed to be discarded after use. The multi-use glass vial option contains 10.5 mL of drug, of which 10 mL is administered and the remainder is assumed to be discarded after use.

Packaging quantities were measured directly for the Prefilled ApiJect Injector and derived from samples for the glass vial and prefilled syringe options. Inventory data for metallized film (Al on PET) are gathered from literature values reported in Bayus *et al*. (2016).[14]

5.3. Life Cycle Impact Assessment

Flows from the life cycle inventory are classified and characterized into measures of environmental impact in the life cycle impact assessment (LCIA) phase of LCA. We apply for LCIA modeling the US Environmental Protection Agency (EPA) Tool for Reduction and Assessment of Chemical and other Environmental Impacts (TRACI) impact assessment model using a midpoint (physical) system perspective.[15] This means that environmental impacts are expressed using metrics and indicators that represent physical quantities and environmental changes, as opposed to an endpoint perspective that uses metrics that represent health or economic damages. The optional normalization and weighting steps of LCIA are not performed and no value choices are applied.

TRACI is widely used in industry and academic research in the US for measuring the environmental impacts identified at outset of production processes and facilities. TRACI is a consensus method that covers ten impact categories including global warming, ozone depletion, fossil fuel depletion, respiratory effects and smog (related to air pollution), acidification and eutrophication (related to water pollution), and human toxicity (cancer and non-cancer effects) and eco-toxicity. These ten impact categories represent specific areas of assessment that together attempt to provide a comprehensive understanding of the environmental performance of a product. The selection of impact categories is in line with internationally accepted environmental impact category indicators. The TRACI 2.2 method is an official model of the U.S. Government and has been extensively peer-reviewed, and its choice of impact categories was originally vetted by the USEPA Science Advisory Board. In addition, we also compare direct water withdrawals (i.e., gross water usage in the foreground system, not life cycle-based) across product options.

Each impact category uses a single substance called a reference substance to assess the relative impact of all the various emissions that affect that aspect of environmental quality. The effect of each emission is scaled to that of the reference substance and then summed to find the category indicator results. For example, the radiative forcing of each greenhouse gas emission is scaled to that of carbon dioxide and summed to find the total climate change impacts quantified in carbon dioxide equivalents (CO_2-eq) using IPCC 2021 AR6 values for 100-year global warming potential GWP_{100}. Further information on the reference substances, indicator units, and characterization models used to calculate characterization factors can be found in the TRACI model documentation and website.[15]

The TRACI method does not include modeling of biogenic carbon and all carbon removals are thus assumed to be balanced by non-fossil emissions of carbon dioxide following end-of-life disposition of carbon-containing materials of biogenic origin (e.g., paperboard).

The LCIA results are presented consistently scaled to the functional unit (delivery of a single 1 mL dose) across all product alternatives, with comparisons and contribution analysis in order to fulfill the goals of the study.

The LCIA results are relative expressions and do not predict impacts on category endpoints, the exceeding of thresholds, safety margins or risks.

5.4. Interpretation

5.4.1. Sensitivity and Uncertainty Modeling

All LCA models are sensitive to the various assumptions of both foreground (measured) and background (supply chain) data that are used. This analysis includes two common techniques for testing the robustness of LCA models. First, sensitivity analysis is used to test individual modeling assumptions to see if they substantially affect the final results and rank order of preference among the product options. Here we test the following assumptions and re-run the analysis with revised parameter values:

- Electricity flows for the ApiJect options, changed from US SERC and Korea grid locations to the global average medium voltage;
- Wastage rate of the finished glass vials and prefilled syringe options, changed from 5% baseline to 15%;
- Transportation distances for all options, increased by 1000 km from default global market transport distances;
- Distribution transport mode for all options, changed from truck to plane;
- Waste management route for all options, changed from landfilling to incineration.

Second, Monte Carlo simulations are conducted for each product system to combine individual parameter uncertainties up to the overall model results by repeatedly sampling from each parameter's probability distribution and re-running the analysis 1,000 times. This approach provides a 90% confidence interval in the results for each product option.

Finally, model sensitivity was tested by conducting the LCIA phase with the ReCiPe 2016 midpoint method[16] and comparing with the TRACI 2.2 results.

5.4.2. Study Limitations

This LCA study has the following limitations, which must be considered when interpreting the results:

- Primary data for the Prefilled ApiJect Injector reflect current production locations, which may shift in the future.
- Results for the glass vial and prefilled syringe alternative options reflect global average production locations, rather than specific geographic locations.
- All options are assumed to be single-use, with no recycling or reuse of any of the components, except for the pre-consumer and post-consumer packaging material;
- Generic transportation and waste management data sets are used, with alternative scenarios for each to investigate sensitivity of the results.
- Manufacturing data for the glass vials and prefilled syringes are from literature rather than from primary data and may deviate from quantities and processes used at a specific production site.
- Manufacturing data for the glass vials and prefilled syringes were scaled from literature values to typical equipment sizes; scaling of electricity, steam, and ethylene oxide flows

were done using typical process scale-up equations with an exponent value of less than one, rather than linearly, and are therefore conservative estimates.

- The TRACI 2.2 life cycle impact assessment model is specific to the United States.
- The TRACI 2.2 life cycle impact assessment model is limited to ten categories of environmental impact and does not include all possible environmental compartments (e.g., differentiation between freshwater, coastal, and marine eutrophication), or environmental issues of emerging concern such as spread of novel entities (e.g., microplastics) or endocrine disruption.

6. RESULTS AND DISCUSSION

6.1. Global Warming

6.1.1. Baseline Results

Figure 7 shows the global warming results for the baseline modeling scenario for each drug delivery option. Per 1 mL dose, the Prefilled ApiJect Injector has the lowest global warming (life cycle greenhouse gas emissions). In comparison, the single-dose glass vial is ~125% higher, the prefilled syringe luer type is ~100% higher, the prefilled syringe staked type is 75% higher, and the multi-dose glass vial is 66% higher. Error bars in Figure 7 denote the 90% confidence interval (5^{th} percentile – 95^{th} percentile) from the Monte Carlo simulations. The complete lack of overlap in the confidence intervals shows a statistically significant difference between the ApiJect results and those for the other drug delivery options.

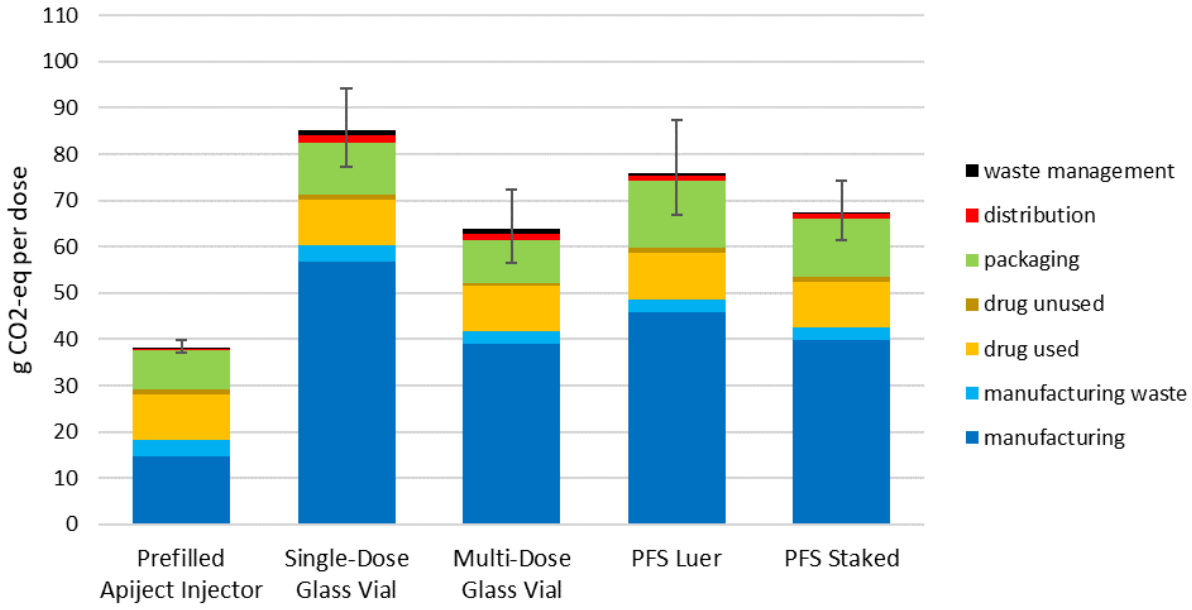

Figure 7. CO_2e emissions results per 1 mL dose for each drug delivery system, measured in grams of carbon dioxide equivalents (g CO_2-eq). Error bars denote the 90% confidence interval from the Monte Carlo simulations.

6.1.2. Contribution Analysis

For all options, the manufacturing step makes the largest contribution to emissions, comprising both emissions from manufacturing energy use as well emissions in the supply chains of all materials. These supply chain emissions include those from extraction of fossil fuels to produce monomers and the polymerization to polymers, and emissions which arise from the melting and purification of the borosilicate glass.

The BFS manufacturing process contributes approximately 15 g CO_2-eq per dose versus 57 g CO_2-eq per dose for the single-dose glass vials. While the life cycle GHG emissions factor for unformed polyethylene and borosilicate glass are similar in the ecoinvent database (2.41 kg CO_2/kg LDPE versus 2.46 kg CO_2/kg borosilicate glass), the single-dose glass vial has approximately 3x the mass of the ApiJect BFS container. The multi-drug glass vial, however, amortizes its heavier mass over the ten doses it provides, and therefore has a smaller per-dose mass than the BFS container. Additionally, the vials undergo annealing, washing, and sterilization prior to drug filling, whereas the BFS containers are filled during the molding process in a sterile environment. Another important material difference between the two systems is that the glass vials each require a separate syringe and two needle assemblies (for dose preparation and drug administration, per dose) whereas the ApiJect system only requires one needle assembly (for administration). Importantly, the polypropylene syringe barrel is fairly heavy, weighing 25% more than the single-dose glass vial itself and with a higher emissions factor (3.44 kg CO_2/kg PP). Overall, the single-dose glass vial (including the rubber stopper, cover disc, and aluminum crimp cap) contribute only 40% to the manufacturing impacts, while the syringe and needle assemblies contribute the 60% majority of manufacturing GHG emissions.

Compared to the prefilled syringe options, BFS manufacturing again has several material advantages. First, the BFS containers are ~50% lighter than the glass syringes. Second, whereas the syringes undergo annealing, washing, ethylene oxide sterilization, and siliconization, the BFS containers require only molding. The electricity required for the ethylene oxide sterilization of the prefilled syringes is by far the largest contributor among these processing steps, contributing more than 10 g CO_2e per 1 mL dose, more even than the glass syringes themselves.

Manufacturing waste includes both material that is used but not incorporated into the final product (such as the polyethylene cut-outs from the BFS process line) as well as any filled drug packaging that does not pass inspection and must be destroyed. The proportional contribution of manufacturing waste for the glass vials and prefilled syringes is ~4% but 9% for the Prefilled ApiJect Injector due to the polyethylene waste. Manufacturing waste can also be further reduced through process improvement efforts.

The drug itself makes a non-negligible contribution to overall emissions, but drug-related emissions are highly variable depending on the active pharmaceutical ingredient (API) and diluent used. This analysis used a generic drug average of 10 kg CO_2-eq per kg of drug that was consistent across each of the delivery devices in the scope of this analysis; however, Parvatker *et al*. found that global warming results for APIs of anesthetic drugs ranged over three orders of magnitude. Therefore, for delivery of carbon-intensive drugs whose syntheses have low overall yields and involve numerous steps, emissions associated with the drug may be much higher than the average value used here and may be relatively more important to the overall results.

Primary, secondary, and tertiary packaging are also important contributors to global warming of the Prefilled ApiJect Injector, comprising 21% of life cycle greenhouse gas emissions. Approximately half of this amount is due to the primary metallized film packaging, assumed to be aluminum on PET film. Aluminum is extremely energy intensive to produce, particularly the refining of alumina (AlO) to aluminum metal, which drives the carbon emissions of the primary packaging. Packaging for the glass vials are boxboard and corrugated cardboard and (for the needles) polyethylene film that have relatively lower embodied emissions.

The final distribution of the drugs from manufacturing to point of use is a small (1%) contributor to emissions (assumed to be 500 km by truck in the baseline scenario). Emissions from landfilling of the used packaging materials are also small (1%).

Detailed contribution analysis results are provided in Appendix A in Tables A1-A5. A percentage contribution summary results is provided in Table A6.

6.2. Direct Water Use

The Prefilled ApiJect Injector manufacturing process uses a minimal amount of water. Specifically, as BFS containers are made and filled in a single step there is no need for a washing or sterilization process as with other primary containers, and water is used only for cleaning equipment. When amortizing the water used for cleaning over all the doses manufacturing during that equipment's run time, the total direct water use for the Prefilled ApiJect Injector was found to be 6.4 mL of water per 1 mL dose. In comparison, for both glass vials and glass prefilled syringes, ultrapure water is used for washing the glass and sterilizing various components. Figure 8 compares the direct water use for each option. Because the water used for the multi-dose glass vial is allocated across 10 doses, its results are relatively low compared to the single-dose glass vial and the prefilled syringes. By far (>95%) the most water is used for the sterilization steps.

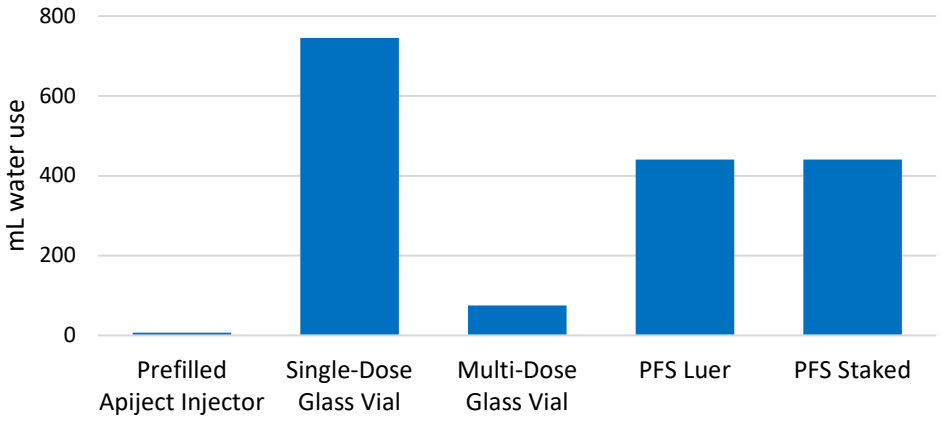

Figure 8. Direct water use per 1 mL dose for each drug delivery system, measured in milliliters (mL) of freshwater use.

6.3. Additional Impact Categories

The Prefilled ApiJect Injector has the lowest environmental impact across all 10 impact categories in the TRACI 2.2 method. Figure 9 shows the full life cycle impact assessment results, shown as a percentage of the maximum result in each impact category. The ApiJect results are between 20-45% of the maximum value, with the exception of ozone depletion where they are only 2% of the maximum value. For most impact categories, the single-use glass vial system has the highest results, largely due to its greater material weight. But for ozone depletion, the prefilled syringes have an order of magnitude higher results. This is due to ozone depleting substances emitted during the production of PVC used for packaging (17% of the total) and the silicone material (polydimethylsiloxane) used to treat the inside of the glass syringe barrel (81% of the total), which is particularly surprising given the small quantity that is used, only 0.6 mg per 1 mL syringe. Quantitative results for all TRACI 2.2 impact categories are provided in Appendix A in Table A7.

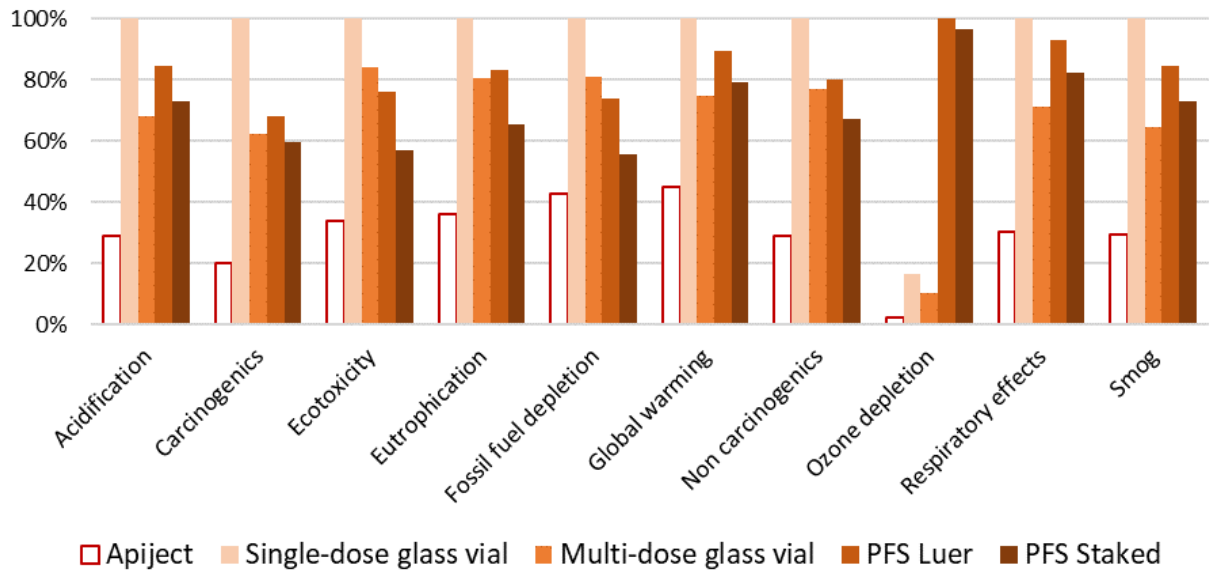

Figure 9. Relative life cycle impact assessment results across TRACI 2.2 impact categories.

6.4. Sensitivity Analysis

Life cycle assessment results can be sensitive to certain modeling parameters. Figure 10 shows the global warming results using alternate modeling scenarios described in Section 5.4. None of the alternate modeling scenarios changes the rank order of the comparative results. Generalizing the location of ApiJect's production and using global average carbon intensity of electricity increases the ApiJect results by 4%. Changing the wastage rate of the filled glass vials and prefilled syringes increases the global warming results for those options by approximately 10% in every case. Using actual supplier distances and changing the transportation mode of distribution to air makes little difference to the results (<3% change).

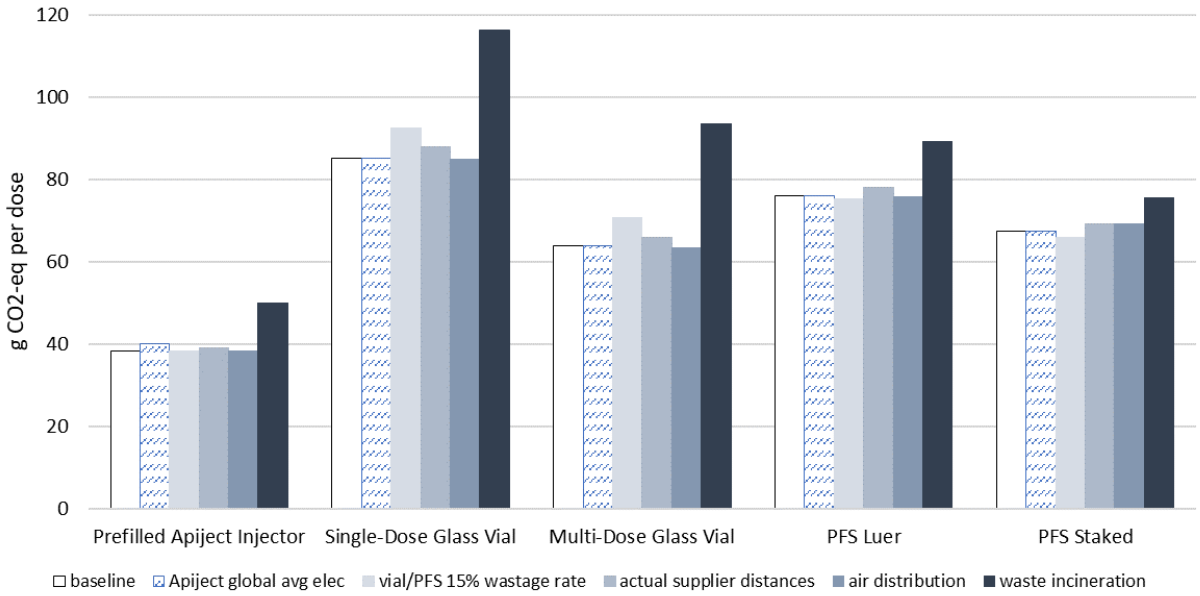

Figure 10. Global warming results per 1 mL dose for each drug delivery system, measured in grams of carbon dioxide equivalents (g CO_2-eq) across alternate modeling scenarios.

The most influential modeling assumption in the sensitivity analysis relates to the waste management route. Incineration of packaging materials at end of life rather than landfill disposal results in a marked increase for all options. For the Prefilled ApiJect Injector, the packaging film and all the components except the needle cannula are forms of fossil-fuel derived plastic that are converted to carbon dioxide during combustion, and end-of-life incineration increases carbon emission results by 32%. The two glass vial options have plastic components for both the dose preparation and application needles and rubber stoppers whose incineration increases their emissions even more than for the ApiJect option in absolute terms. Even though the vessels for the drug are glass instead of polyethylene plastic in the ApiJect case, the overall mass of plastic used in the single-dose glass vial system is more than double that of the Prefilled ApiJect Injector: 10.5 g of plastic versus 4.6 g of plastic. Only, for the staked prefilled syringe is the mass of plastic components less than that of the Prefilled ApiJect Injector, thanks to its relative simplicity.

Considering model sensitivity, results using the ReCiPe (2016) midpoint (H) impact assessment method found essentially the same pattern of results as for TRACI shown in Figure 9, with the ApiJect system having 25-40% of the impacts of the single-dose glass vial alternative, except in the case of ozone depletion where the pre-filled syringes have the highest impacts. The full ReCiPe results are provided in Appendix Table A8.

6.5. Uncertainty Analysis

Monte Carlo simulation was used to construct 90% confidence intervals for each of the product options and impact categories. Table 3 shows these confidence intervals normalized by their respective mean values (akin to a coefficient of variation but for the 5th and 95th percentiles rather than the standard deviation).

Table 3. Confidence intervals for all product options and impact categories, normalized by respective means.

	Prefilled ApiJect Injector		**Single-dose Glass Vial**		**Multi-dose Glass Vial**		**Prefilled Syringe Luer type**		**Prefilled Syringe Staked type**	
Percentile>	**5%**	**95%**	**5%**	**95%**	**5%**	**95%**	**5%**	**95%**	**5%**	**95%**
Impact Category										
Acidification	-14%	15%	-11%	11%	-10%	12%	-8%	10%	-10%	11%
Carcinogenics	-86%	269%	-78%	179%	-86%	221%	-88%	213%	-88%	182%
Ecotoxicity	-68%	136%	-70%	141%	-66%	141%	-66%	136%	-65%	143%
Eutrophication	-48%	80%	-48%	85%	-49%	77%	-47%	78%	-47%	73%
Fossil fuel depletion	-17%	19%	-12%	14%	-13%	15%	-8%	8%	-9%	9%
Global warming	-13%	15%	-9%	10%	-10%	12%	-11%	14%	-8%	10%
Non-carcinogenics	-59%	100%	-85%	-22%	-64%	76%	-60%	92%	-74%	59%
Ozone depletion	-40%	60%	-33%	50%	-33%	57%	-20%	22%	-19%	22%
Respiratory effects	-13%	14%	-12%	15%	-12%	15%	-11%	14%	-12%	15%
Smog	-14%	16%	-12%	13%	-9%	12%	-10%	13%	-12%	13%

As is typical, the global warming results have the smallest uncertainties due to the high confidence assigned to the GWP_{100} characterization factors, while the toxicity-related categories (carcinogenics, non-carcinogenics, and ecotoxicity) all have 95th percentile values that can be >200% of the mean value due the low confidence assigned to the USEtox characterization factors that underpin those results. This LCA report focuses on GHG emissions and direct water use but presents results for all impact categories. More caution should be taken in interpreting the results for impact categories with large confidence intervals.

6.6. Completeness Check

A completeness check was conducted following the life cycle inventory and life cycle impact assessment phases. All flows that were considered within the system boundary were included in the inventory modeling. Analysis of the LCIA Checks tab within open LCA found that the only notable non-characterized flows were non-fossil emissions of carbon dioxide, which are not considered to balance carbon removals in the TRACI method and are thus not characterized.

7. CONCLUSIONS

The life cycle assessment has produced specific and definitive findings. showing that the Prefilled ApiJect Injector has the lowest global warming, with the other options having 65-125% higher GHG emissions per 1 mL dose, depending on the option analyzed, and that these results are statistically significant. The analysis followed ISO 14040 and 14044 standards and used a combination of direct measurements and life cycle inventory data from well-known commercial ecoinvent database, with impact assessment following the TRACI 2.2 method of the USEPA.

Direct water use for the Prefilled ApiJect Injector was found to be <10 mL per dose, which is lower than the other options by approximately 1-2 orders of magnitude. For other impact categories in the TRACI 2.2 impact assessment method, the ApiJect results are also consistently the lowest among the five options.

The analysis also reveals opportunities for process improvement that would help lower the environmental impacts of the Prefilled ApiJect Injector even further. These include procurement of low-carbon electricity, reducing manufacturing waste, and reducing packaging materials where possible.

APPENDIX A: Life Cycle Impact Assessment Numerical Results

Table A1. Contribution analysis detail for GHG emissions for Prefilled ApiJect Injector.

Process	**g CO_2e**	**% of total GHG emissions**
Manufacturing + Fill-Finish		
BFS container	3.5	9.1%
Needle Safety Feature	3.8	9.8%
Needle Cap	3.7	9.7%
Needle Cannula	0.3	0.7%
Connector	2.2	5.8%
BFS machine	0.8	2.2%
Chiller energy	0.1	0.4%
Optical inspection energy	0.2	0.6%
Drug used	10.0	26.1%
Drug unused	1.0	2.6%
Packaging		
Foil wrapping	4.0	10.5%
Carton	2.5	6.4%
Paper insert	0.3	0.7%
Cardboard shipper	1.4	3.7%
Pallet	0.2	0.5%
Production waste		
BFS material wastage	3.0	7.8%
Inspection wastage	0.5	1.4%
Waste management	0.4	1.1%
Distribution	0.3	0.8%

Table A2. Contribution analysis detail for GHG emissions for single-dose glass vial system.

Process	**g CO_2e**	**% of total GHG emissions**
Manufacturing + Fill-Finish		
Vial Stopper	1.3	1.5%
Vial Stopper sterilization	1.1	1.3%
Crimp Cap - cover disc	0.8	0.9%
Crimp Cap - metal crimp	1.8	2.1%
Vial Production & Preparation	16.4	19.2%
Vial sterilization	1.1	1.3%
Syringe Barrel	19.3	22.7%
Syringe plunger rod	3.3	3.9%
Syringe plunger stopper	0.3	0.4%
Dose Prep Needle - Cannula	0.4	0.5%
Dose Prep Needle - Needle Cover	1.5	1.7%
Dose Prep Needle - Needle Hub	0.7	0.8%
Admin Needle - Cannula	0.2	0.2%
Admin Needle - Needle Cover	3.9	4.5%
Admin Needle - Needle Safety Feature	3.2	3.8%
Admin Needle - Needle Hub	1.5	1.8%
Drug used	10.0	11.7%
Drug unused	1.0	1.2%
Packaging		
Vial - paperboard	3.8	4.5%
Blister packs - paper	1.0	1.2%
Blister packs - PP	4.8	5.7%
Cardboard shipper	1.4	1.6%
Pallet	0.2	0.2%
Manufacturing Waste	3.6	4.2%
Waste management	1.2	1.4%
Distribution	1.4	1.7%

Table A3. Contribution analysis detail for GHG emissions for multi-dose glass vial system.

Process	**g CO_2e**	**% of total GHG emissions**
Manufacturing + Fill-Finish		
Vial Stopper	0.5	0.8%
Vial Stopper sterilization	0.1	0.2%
Crimp Cap - cover disc	0.2	0.3%
Crimp Cap - metal crimp	0.3	0.5%
Vial Production & Preparation	3.5	5.5%
Vial sterilization	0.1	0.2%
Syringe Barrel	19.3	30.3%
Syringe plunger rod	3.3	5.2%
Syringe plunger stopper	0.3	0.5%
Dose Prep Needle - Cannula	0.4	0.6%
Dose Prep Needle - Needle Cover	1.5	2.3%
Dose Prep Needle - Needle Hub	0.7	1.1%
Admin Needle - Cannula	0.2	0.3%
Admin Needle - Needle Cover	3.9	6.1%
Admin Needle - Needle Safety Feature	3.2	5.1%
Admin Needle - Needle Hub	1.5	2.4%
Drug used	10.0	15.7%
Drug unused	0.5	0.8%
Packaging		
Vial - paperboard	1.9	3.0%
Blister packs - paper	1.0	1.6%
Blister packs - PP	4.8	7.6%
Cardboard shipper	1.4	2.2%
Pallet	0.2	0.3%
Manufacturing Waste	2.6	4.1%
Waste management	1.1	1.7%
Distribution	1.1	1.7%

Table A4. Contribution analysis detail for GHG emissions for prefilled syringe luer type.

Process	**g CO_2e**	**% of total GHG emissions**
Manufacturing + Fill-Finish		
Barrel Production & Preparation	13.1	17.3%
Barrel sterilization	12.7	16.8%
Rigid Cap	2.9	3.8%
Tip Cap	1.3	1.7%
Plunger Stopper	0.5	0.7%
Plunger Rod	5.2	6.9%
Plunger Rod sterilization	1.1	1.4%
Admin Needle - Cannula	0.2	0.2%
Admin Needle - Needle Cover	3.9	5.1%
Admin Needle - Needle Safety Feature	3.2	4.3%
Admin Needle - Needle Hub	1.5	2.0%
Drug used	10.0	13.2%
Drug unused	1.0	1.3%
Packaging		
PFS packaging - PVC	10.7	14.1%
PFS packaging - paper	0.3	0.4%
Blister packs - paper	0.3	0.5%
Blister packs - PP	1.6	2.1%
Cardboard shipper	1.4	1.9%
Pallet	0.2	0.3%
Manufacturing Waste	3.0	3.9%
Waste management	0.5	0.7%
Distribution	1.1	1.4%

Table A5. Contribution analysis detail for GHG emissions for prefilled syringe staked type.

Process	**g CO_2e**	**% of total GHG emissions**
Manufacturing + Fill-Finish		
Barrel Production & Preparation	11.5	17.1%
Barrel sterilization	12.7	18.9%
Staked Needle	0.2	0.3%
Plunger Stopper	0.5	0.8%
Plunger Rod	5.2	7.8%
Plunger Rod sterilization	1.1	1.6%
Rubber tip cover	1.3	1.9%
Rigid cover	7.3	10.8%
Drug used	10.0	14.8%
Drug unused	1.0	1.5%
Packaging		
PFS packaging - PVC	10.7	15.8%
PFS packaging - paper	0.3	0.5%
Cardboard shipper	1.4	2.1%
Pallet	0.2	0.3%
Manufacturing Waste	2.7	4.0%
Waste management	0.3	0.5%
Distribution	0.9	1.3%

Table A6. Contribution analysis percentage summary for GHG emissions for all product options.

	Prefilled ApiJect Injector	**Single-Dose Glass Vial**	**Multi-Dose Glass Vial**	**PFS Luer**	**PFS Staked**
Manufacturing	38%	67%	61%	60%	59%
Manufacturing waste	9%	4%	4%	4%	4%
Drug used	26%	12%	16%	13%	15%
Drug unused	3%	1%	1%	1%	1%
Packaging	22%	13%	15%	19%	19%
Distribution	1%	2%	2%	1%	1%
Waste management	1%	1%	2%	1%	0%
Total	**100%**	**100%**	**100%**	**100%**	**100%**

Table A7. Quantitative results comparing five product options across all TRACI 2.2 impact categories.

Impact Category	**Unit**	**Prefilled ApiJect Injector**	**Single-Dose Glass Vial**	**Multi-Dose Glass Vial**	**PFS Luer**	**PFS Staked**
Acidification	kg SO_2 eq	9.00E-05	3.11E-04	2.11E-04	2.63E-04	2.27E-04
Carcinogenics	CTUh	7.80E-10	3.88E-09	2.42E-09	2.64E-09	2.32E-09
Ecotoxicity	CTUe	3.98E-01	1.17E+00	9.88E-01	8.91E-01	6.68E-01
Eutrophication	kg N eq	1.20E-04	3.33E-04	2.68E-04	2.77E-04	2.18E-04
Global warming	kg CO_2 eq	3.83E-02	8.51E-02	6.37E-02	7.59E-02	6.73E-02
Non carcinogenics	CTUh	4.76E-09	1.64E-08	1.26E-08	1.31E-08	1.10E-08
Ozone depletion	kg CFC-11 eq	4.59E-10	3.72E-09	2.29E-09	2.26E-08	2.18E-08
Respiratory effects	kg $PM_{2.5}$ eq	1.98E-05	6.53E-05	4.63E-05	6.07E-05	5.38E-05
Smog	kg O_3 eq	1.30E-03	4.46E-03	2.87E-03	3.77E-03	3.24E-03

Table A8. Quantitative results comparing five product options across all ReCiPe (2016) midpoint (H) impact categories.

Impact Category	Unit	Prefilled ApiJect Injector	Single-Dose Glass Vial	Multi-Dose Glass Vial	PFS Luer	PFS Staked
Acidification: terrestrial	kg SO2-eq	7.57E-05	2.46E-04	1.80E-04	2.02E-04	1.78E-04
Climate change	kg CO2-eq	2.94E-02	7.98E-02	6.19E-02	6.73E-02	5.94E-02
Ecotoxicity: freshwater	kg 1,4-DCB-eq	1.02E-03	2.56E-03	2.28E-03	1.92E-03	1.47E-03
Ecotoxicity: marine	kg 1,4-DCB-eq	1.44E-03	3.64E-03	3.24E-03	2.73E-03	2.09E-03
Ecotoxicity: terrestrial	kg 1,4-DCB-eq	1.62E-02	4.73E-02	3.85E-02	3.15E-02	2.88E-02
Energy resources: non-renewable, fossil	kg oil-eq	1.37E-02	3.42E-02	2.88E-02	2.56E-02	2.01E-02
Eutrophication: freshwater	kg P-eq	9.64E-06	2.26E-05	1.75E-05	2.02E-05	1.71E-05
Eutrophication: marine	kg N-eq	2.61E-06	6.07E-06	5.52E-06	4.65E-06	3.59E-06
Human toxicity: carcinogenic	kg 1,4-DCB-eq	7.62E-04	2.62E-03	1.68E-03	1.76E-03	1.57E-03
Human toxicity: non-carcinogenic	kg 1,4-DCB-eq	2.61E-02	6.72E-02	5.62E-02	5.21E-02	4.15E-02
Ionising radiation	kBq Co-60-eq	8.36E-05	1.36E-04	1.09E-04	1.32E-04	1.14E-04
Land use	m2*a crop-eq	1.56E-03	1.79E-03	1.69E-03	1.63E-03	1.60E-03
Material resources: metals/minerals	kg Cu-eq	3.02E-05	1.49E-04	1.05E-04	4.42E-05	4.04E-05
Ozone depletion	kg CFC-11-eq	6.79E-09	2.23E-08	1.70E-08	2.50E-08	2.43E-08
Particulate matter formation	kg PM2.5-eq	3.94E-05	1.23E-04	9.14E-05	1.06E-04	9.42E-05
Photochemical oxidant formation: human health	kg NOx-eq	6.04E-05	1.94E-04	1.34E-04	1.57E-04	1.37E-04
Photochemical oxidant formation: terrestrial ecosystems	kg NOx-eq	6.35E-05	2.00E-04	1.39E-04	1.61E-04	1.39E-04
Water use (life cycle)	m3	2.59E-04	7.01E-04	5.63E-04	5.72E-04	4.84E-04

APPENDIX B: Life Cycle Inventory Data

Table B1. Inventory data and background data sets for production of Prefilled ApiJect Injector.

Process	Input Flow	Qty	Unit	Ecoinvent processes
BFS container	Medical grade LDPE	1.450	g	- polyethylene, low density, granulate//[GLO] market for polyethylene, low density, granulate
Needle safety feature	Polypropylene	1.097	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Needle cap	Polypropylene	1.086	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Needle cannula	Stainless steel (SUS 304), lubricant	0.056	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Connector	Polypropylene, Colorant	0.646	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
BFS energy	Electricity	0.0029	kWh	- USEPA eGRID 2021 SRVC
Chiller energy	Electricity	0.0005	kWh	- USEPA eGRID 2021 SRVC
Assembly energy	Electricity	.006	kWh	- electricity medium voltage//[KR] market for electricity, medium voltage
Drug	Generic drug	1.1	g	- Representative value of 10 kg CO_2-eq per kg of drug from Parvatker *et al.*; global average datasets for inputs of heat and electricity
Optical inspection energy	Electricity	0.0007	kWh	- USEPA eGRID 2021 SRVC
Packaging primary	Metallized film	0.360	g	- Inventory data scaled from Bayus *et al*. (2016)

Process	Input Flow	Qty	Unit	Ecoinvent processes
Paper insert	Bleached paper	0.268	g	- paper, woodfree, uncoated//[RoW] paper production, woodfree, uncoated, at integrated mill
Packaging secondary	Boxboard	0.964	g	- carton board box production, with offset printing//[GLO] market for carton board box production, with offset printing
Packaging tertiary	Cardboard	1.377	g	- corrugated board box//[RoW] market for corrugated board box
Packaging pallet	Softwood lumber	0.785	g	- sawnwood, board, softwood, raw, dried (u=10%)//[CA-QC] board, softwood, raw, kiln drying to u=10%
Distribution	Truck transport	2.347	kg-km	- transport, freight, lorry, unspecified//[GLO] market group for transport, freight, lorry, unspecified
Landfill disposal	Waste plastic	4.638	g	- waste polypropylene//[RoW] treatment of waste polypropylene, sanitary landfill
	Waste glass / metal	0.0561	g	- waste glass//[GLO] treatment of waste glass, sanitary landfill

Table B2. Inventory data and background data sets for production of single-dose glass vial system.

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Glass vial	Borosilicate Type I glass	4.466	g	- glass tube, borosilicate, at plant
	Oxygen	1.266	g	- oxygen, liquid//[RoW] air separation, cryogenic
	Heat	51.84	kJ	- heat, natural gas, at industrial furnace low-NOx >100kW
Glass vial washing	DI water	0.300	mL	- water, deionized//[RoW] market for water, deionized
Glass vial sterilization	Heat	0.001	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	DI water	372.4	mL	- water, deionized//[RoW] market for water, deionized
Vial stopper	latex-free bromobutyl rubber	0.485	g	- synthetic rubber, at plant
Vial stopper sterilization	Heat	0.001	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	DI water	372.4	mL	- water, deionized//[RoW] market for water, deionized
Crimp cap	Polypropylene	0.225	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
	Aluminum	0.197	g	- aluminium, production mix, at plant - sheet rolling, aluminium
Syringe barrel	Polypropylene	5.62	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Syringe plunger rod	Polypropylene	0.956	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Syringe plunger stopper	Synthetic polyisoprene	0.129	g	- synthetic rubber, at plant
Dose Preparation Needle - Cannula	Stainless steel, type 304	0.089	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Dose Preparation Needle - Needle Cover	Polypropylene	0.429	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Dose Preparation Needle - Needle Hub	Polypropylene	0.200	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Cannula	Stainless steel (SUS 304), lubricant	0.042	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Administration Needle - Needle Cover	Polypropylene	1.126	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Needle Safety Feature	Polypropylene	0.945	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Needle Hub	Polypropylene	0.437	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Assembly energy	Electricity	.012	kWh	- electricity medium voltage//[GLO] market group for electricity, medium voltage
Drug	Generic drug	1.1	g	- Representative value of 10 kg CO_2-eq per kg of drug from Parvatker *et al*.; global average datasets for inputs of heat and electricity
Packaging – syringe + needles	Polyethylene film	1.41	g	- polyethylene, low density, granulate//[GLO] market for polyethylene, low density, granulate

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
	Medical grade paper	1.02	g	- paper, woodfree, uncoated//[RoW] paper production, woodfree, uncoated, at integrated mill
Packaging - vials	Boxboard	1.5	g	- carton board box production, with offset printing//[GLO] market for carton board box production, with offset printing
Packaging tertiary	Cardboard	1.38	g	- corrugated board box//[RoW] market for corrugated board box
Packaging pallet	Softwood lumber	0.785	g	- sawnwood, board, softwood, raw, dried (u=10%)//[CA-QC] board, softwood, raw, kiln drying to u=10%
Distribution	Truck transport	21.43	kg-km	- transport, freight, lorry, unspecified//[GLO] market group for transport, freight, lorry, unspecified
Landfill disposal	Waste plastic	11.96	g	- waste polypropylene//[RoW] treatment of waste polypropylene, sanitary landfill
	Waste glass / metal	4.794	g	- waste glass//[GLO] treatment of waste glass, sanitary landfill

Table B3. Inventory data and background data sets for production of multi-dose glass vial system.

Process	# doses	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Glass vial	10	Borosilicate Type I glass	9.568	g	- glass tube, borosilicate, at plant
	10	Oxygen	2.712	g	- oxygen, liquid//[RoW] air separation, cryogenic
	10	Heat	111.1	kJ	- heat, natural gas, at industrial furnace low-NOx >100kW
Glass vial washing	10	DI water	1.0000	mL	- water, deionized//[RoW] market for water, deionized
Glass vial sterilization	10	Heat	0.001	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	10	DI water	372.4	mL	- water, deionized//[RoW] market for water, deionized
Vial stopper	10	latex-free bromobutyl rubber	1.809	g	- synthetic rubber, at plant
Vial stopper sterilization	10	Heat	0.001	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	10	DI water	372.4	mL	- water, deionized//[RoW] market for water, deionized
Crimp cap	10	Polypropylene	0.521	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
	10	Aluminum	0.376	g	- aluminium, production mix, at plant - sheet rolling, aluminium
Syringe barrel	1	Polypropylene	5.62	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Syringe plunger rod	1	Polypropylene	0.956	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding

Process	# doses	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Syringe plunger stopper	1	Synthetic polyisoprene	0.129	g	- synthetic rubber, at plant
Dose Preparation Needle - Cannula	1	Stainless steel, type 304	0.089	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Dose Preparation Needle - Needle Cover	1	Polypropylene	0.429	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Dose Preparation Needle - Needle Hub	1	Polypropylene	0.200	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Cannula	1	Stainless steel (SUS 304), lubricant	0.042	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Administration Needle - Needle Cover	1	Polypropylene	1.126	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Needle Safety Feature	1	Polypropylene	0.945	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Needle Hub	1	Polypropylene	0.437	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Assembly energy	1	Electricity	.012	kWh	- electricity medium voltage//[GLO] market group for electricity, medium voltage
Drug	1	Generic drug	1.05	g	- Representative value of 10 kg CO_2-eq per kg of drug from Parvatker *et al.*; global average datasets for inputs of heat and electricity

Process	# doses	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Packaging – syringe + needles	1	Polyethylene film	1.41	g	- polyethylene, low density, granulate//[GLO] market for polyethylene, low density, granulate
	1	Medical grade paper	1.02	g	- paper, woodfree, uncoated//[RoW] paper production, woodfree, uncoated, at integrated mill
Packaging - vials	1	Boxboard	0.75	g	- carton board box production, with offset printing//[GLO] market for carton board box production, with offset printing
Packaging tertiary	1	Cardboard	1.38	g	- corrugated board box//[RoW] market for corrugated board box
Packaging pallet	1	Softwood lumber	0.785	g	- sawnwood, board, softwood, raw, dried (u=10%)//[CA-QC] board, softwood, raw, kiln drying to u=10%
Distribution	1	Truck transport	16.54	kg-km	- transport, freight, lorry, unspecified//[GLO] market group for transport, freight, lorry, unspecified
Landfill disposal	1	Waste plastic	11.48	g	- waste polypropylene//[RoW] treatment of waste polypropylene, sanitary landfill
	1	Waste glass / metal	1.125	g	- waste glass//[GLO] treatment of waste glass, sanitary landfill

Table B4. Inventory data and background data sets for production of prefilled syringe luer type.

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Glass syringe barrel	Borosilicate Type I glass	3.584	g	- glass tube, borosilicate, at plant
	Oxygen	1.016	g	- oxygen, liquid//[RoW] air separation, cryogenic
	Heat	41.60	kJ	- heat, natural gas, at industrial furnace low-NOx >100kW
Glass syringe barrel washing	DI water	0.100	mL	- water, deionized//[RoW] market for water, deionized
Glass syringe barrel sterilization and siliconization	Heat	0.015	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	DI water	67.70	mL	- water, deionized//[RoW] market for water, deionized
	Ethylene oxide	1.016	g	- ethylene oxide//[RoW] market for ethylene oxide
	Silicone spray	0.001	g	- polydimethylsiloxane//[GLO] market for polydimethylsiloxane
Rigid cap	Polycarbonate	0.374	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Tip cap	Latex-free bromobutyl rubber	0.492	g	- synthetic rubber, at plant
Syringe plunger rod	Polypropylene	1.523	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Syringe plunger stopper	Latex-free bromobutyl rubber	0.198	g	- synthetic rubber, at plant
Syringe plunger stopper sterilization	Steam sterilization energy	0.001	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	Steam sterilization DI water	372.4	mL	- water, deionized//[RoW] market for water, deionized

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Administration Needle - Cannula	Stainless steel (SUS 304), lubricant	0.042	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Administration Needle - Needle Cover	Polypropylene	1.126	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Needle Safety Feature	Polypropylene	0.945	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Administration Needle - Needle Hub	Polypropylene	0.437	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Assembly energy	Electricity	.006	kWh	- electricity medium voltage//[GLO] market group for electricity, medium voltage
Drug	Generic drug	1.1	g	- Representative value of 10 kg CO_2-eq per kg of drug from Parvatker *et al.*; global average datasets for inputs of heat and electricity
Packaging - PFS	Polyvinyl chloride tray	3.3	g	- polyvinylchloride, bulk polymerised//[GLO] market for polyvinylchloride, bulk polymerised - injection moulding//[GLO] market for injection moulding
	Medical grade paper	0.33	g	- paper, woodfree, uncoated//[RoW] paper production, woodfree, uncoated, at integrated mill
Packaging - needle	Polyethylene film	0.47	g	- polyethylene, low density, granulate//[GLO] market for polyethylene, low density, granulate
	Bleached paper	0.34	g	- paper, woodfree, uncoated//[RoW] paper production, woodfree, uncoated, at integrated mill
Packaging tertiary	Cardboard	1.38	g	- corrugated board box//[RoW] market for corrugated board box

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Packaging pallet	Softwood lumber	0.785	g	- sawnwood, board, softwood, raw, dried (u=10%)//[CA-QC] board, softwood, raw, kiln drying to u=10%
Distribution	Truck transport	5.135	kg-km	- transport, freight, lorry, unspecified//[GLO] market group for transport, freight, lorry, unspecified
Landfill disposal	Waste plastic	5.094	g	- waste polypropylene//[RoW] treatment of waste polypropylene, sanitary landfill
	Waste glass / metal	0.042	g	- waste glass//[GLO] treatment of waste glass, sanitary landfill

Table B5. Inventory data and background data sets for production of prefilled syringe staked type.

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Glass syringe barrel	Borosilicate Type I glass	3.584	g	- glass tube, borosilicate, at plant
	Oxygen	1.016	g	- oxygen, liquid//[RoW] air separation, cryogenic
	Heat	41.60	kJ	- heat, natural gas, at industrial furnace low-NOx >100kW
Glass syringe barrel washing	DI water	0.100	mL	- water, deionized//[RoW] market for water, deionized
Glass syringe barrel sterilization and siliconization	Heat	0.015	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	DI water	67.70	mL	- water, deionized//[RoW] market for water, deionized
	Ethylene oxide	1.016	g	- ethylene oxide//[RoW] market for ethylene oxide
	Silicone spray	0.001	g	- polydimethylsiloxane//[GLO] market for polydimethylsiloxane
Staked needle	Stainless steel (SUS 304), lubricant	0.042	g	- steel, chromium steel 18/8//[GLO] market for steel, chromium steel 18/8 - drawing of pipes, steel
Syringe plunger rod	Polypropylene	1.523	g	- polypropylene, granulate//[GLO] market for polypropylene, granulate - injection moulding//[GLO] market for injection moulding
Syringe plunger stopper	Latex-free bromobutyl rubber	0.198	g	- synthetic rubber, at plant
Syringe plunger stopper sterilization	Steam sterilization energy	0.001	kWh	- electricity, medium voltage//[GLO] market group for electricity, medium voltage
	Steam sterilization DI water	372.4	mL	- water, deionized//[RoW] market for water, deionized
Needle Cover (rubber tip cover)	Latex-free bromobutyl rubber	0.470	g	- synthetic rubber, at plant

Process	Input Flow	Qty	Unit	Ecoinvent LCI data sets
Needle Cover (rigid cover)	Polycarbonate	0.945	g	- polycarbonate//[GLO] market for polycarbonate
Assembly energy	Electricity	.006	kWh	- electricity medium voltage//[GLO] market group for electricity, medium voltage
Drug	Generic drug	1.1	g	- Representative value of 10 kg CO_2-eq per kg of drug from Parvatker *et al.*; global average datasets for inputs of heat and electricity
Packaging - PFS	Polyvinyl chloride tray	3.3	g	- polyvinylchloride, bulk polymerised//[GLO] market for polyvinylchloride, bulk polymerised - injection moulding//[GLO] market for injection moulding
	Medical grade paper	0.33	g	- paper, woodfree, uncoated//[RoW] paper production, woodfree, uncoated, at integrated mill
Packaging tertiary	Cardboard	1.38	g	- corrugated board box//[RoW] market for corrugated board box
Packaging pallet	Softwood lumber	0.785	g	- sawnwood, board, softwood, raw, dried (u=10%)//[CA-QC] board, softwood, raw, kiln drying to u=10%
Distribution	Truck transport	3.177	kg-km	- transport, freight, lorry, unspecified//[GLO] market group for transport, freight, lorry, unspecified
Landfill disposal	Waste plastic	3.135	g	- waste polypropylene//[RoW] treatment of waste polypropylene, sanitary landfill
	Waste glass / metal	0.042	g	- waste glass//[GLO] treatment of waste glass, sanitary landfill

Appendix C: Data Quality Assessment

The Pedigree matrix method used for measuring data quality requires that each flow type is assigned basic uncertainty factors which are then combined using the following equation to calculate a squared geometric standard deviation:

$$SSD_{g95} = \sqrt{exp[\ln(U_1)^2 + \ln(U_2)^2 + \ln(U_3)^2 + \ln(U_4)^2 + \ln(U_5)^2 + \ln(U_6)^2]}$$

where:

U_1: uncertainty factor of reliability

U_2: uncertainty factor of completeness

U_3: uncertainty factor of temporal correlation

U_4: uncertainty factor of geographic correlation

U_5: uncertainty of further technological correlation

The five types of DQI are evaluated according to the Pedigree matrix using scores from 1 to 5, with 1 indicating the lowest uncertainty and 5 indicating the highest uncertainty.

DQI values for each product system are shown in Tables C1-C5.

Pedigree matrix scoring descriptions are shown in Table C6.

Table C1. Data Quality Indicator scores for Prefilled ApiJect Injector.

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
BFS container	1	2	3	2	3
Needle safety feature	1	2	3	2	3
Needle cap	1	2	3	2	3
Needle cannula	1	2	3	2	3
Connector	1	2	3	2	3
BFS energy	1	1	3	1	1
Chiller energy	2	1	3	1	1
Optical inspection energy	2	1	3	1	1
Assembly energy	1	1	1	1	1
Drug	3	1	1	1	3
Packaging primary	1	2	3	2	3
Paper insert	1	2	3	2	3
Packaging secondary	1	2	3	2	3
Packaging tertiary	1	2	3	2	3
Packaging pallet	1	2	3	2	3
Distribution	3	1	3	2	1
Landfill disposal	1	1	3	2	1

Table C2. Data Quality Indicator scores for single-dose glass vial system.

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Glass vial - glass	1	2	3	2	3
Glass vial - oxygen	3	4	3	3	1
Glass vial - heat	3	4	3	3	1
Glass vial washing	3	4	3	3	1
Glass vial sterilization - heat	3	4	1	3	2
Glass vial sterilization - water	3	4	3	3	1
Vial stopper	1	2	3	2	3
Vial stopper sterilization - heat	3	4	1	3	2
Vial stopper sterilization - water	3	4	3	3	1
Crimp cap - PP	1	2	3	2	3
Crimp cap - Al	1	2	3	2	3
Syringe barrel	1	2	3	2	3
Syringe plunger rod	1	2	3	2	3
Syringe plunger stopper	1	2	3	2	3
Dose Preparation Needle - Cannula	1	2	3	2	3
Dose Preparation Needle - Needle Cover	1	2	3	2	3
Dose Preparation Needle - Needle Hub	1	2	3	2	3
Administration Needle - Cannula	1	2	3	2	3

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Administration Needle - Needle Cover	1	2	3	2	3
Administration Needle - Needle Safety Feature	1	2	3	2	3
Administration Needle - Needle Hub	1	2	3	2	3
Assembly energy	3	4	1	3	2
Drug	3	1	1	1	3
Packaging – syringe + needles - PE	1	1	3	2	2
Packaging – syringe + needles - paper	1	1	3	2	2
Packaging - vials	1	1	3	2	2
Packaging tertiary	3	1	3	2	2
Packaging pallet	3	1	3	2	2
Distribution	3	1	3	2	1
Landfill disposal	1	1	3	2	1

Table C3. Data Quality Indicator scores for multi-dose glass vial system.

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Glass vial - glass	1	2	3	2	3
Glass vial - oxygen	3	4	3	3	1
Glass vial - heat	3	4	3	3	1
Glass vial washing	3	4	3	3	1
Glass vial sterilization - heat	3	4	1	3	2
Glass vial sterilization - water	3	4	3	3	1
Vial stopper	1	2	3	2	3
Vial stopper sterilization - heat	3	4	1	3	2
Vial stopper sterilization - water	3	4	3	3	1
Crimp cap - PP	1	2	3	2	3
Crimp cap - Al	1	2	3	2	3
Syringe barrel	1	2	3	2	3
Syringe plunger rod	1	2	3	2	3
Syringe plunger stopper	1	2	3	2	3
Dose Preparation Needle - Cannula	1	2	3	2	3
Dose Preparation Needle - Needle Cover	1	2	3	2	3
Dose Preparation Needle - Needle Hub	1	2	3	2	3
Administration Needle - Cannula	1	2	3	2	3

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Administration Needle - Needle Cover	1	2	3	2	3
Administration Needle - Needle Safety Feature	1	2	3	2	3
Administration Needle - Needle Hub	1	2	3	2	3
Assembly energy	3	4	1	3	2
Drug	3	1	1	1	3
Packaging – syringe + needles - PE	1	1	3	2	2
Packaging – syringe + needles - paper	1	1	3	2	2
Packaging - vials	1	1	3	2	2
Packaging tertiary	3	1	3	2	2
Packaging pallet	3	1	3	2	2
Distribution	3	1	3	2	1
Landfill disposal	1	1	3	2	1

Table C4. Data Quality Indicator scores for prefilled syringe luer type.

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Glass syringe barrel - glass	1	2	3	2	3
Glass syringe barrel - oxygen	3	4	3	3	1
Glass syringe barrel - heat	3	4	1	3	2
Glass syringe barrel washing	3	4	3	3	1
Glass syringe barrel sterilization and siliconization - heat	3	4	1	3	2
Glass syringe barrel sterilization and siliconization – heat – DI water	3	4	3	3	1
Glass syringe barrel sterilization and siliconization – heat – ethylene oxide	3	4	3	3	1
Glass syringe barrel sterilization and siliconization – heat – silicone	3	4	3	3	1
Rigid cap	1	2	3	2	3
Tip cap	1	2	3	2	3
Syringe plunger rod	1	2	3	2	3
Syringe plunger stopper	1	2	3	2	3
Syringe plunger stopper sterilization - heat	3	4	1	3	2

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Syringe plunger stopper sterilization - water	3	4	3	3	1
Administration Needle - Cannula	1	2	3	2	3
Administration Needle - Needle Cover	1	2	3	2	3
Administration Needle - Needle Safety Feature	1	2	3	2	3
Administration Needle - Needle Hub	1	2	3	2	3
Assembly energy	3	4	1	3	2
Drug	3	1	1	1	3
Packaging PFS - PVC	1	1	3	2	2
Packaging PFS - paper	1	1	3	2	2
Packaging needle - PE	1	1	3	2	2
Packaging needle - paper	1	1	3	2	2
Packaging tertiary	3	1	3	2	2
Packaging pallet	3	1	3	2	2
Distribution	3	1	3	2	1
Landfill disposal	1	1	3	2	1

Table C5. Data Quality Indicator scores for prefilled syringe staked type.

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Glass syringe barrel - glass	1	2	3	2	3
Glass syringe barrel - oxygen	3	4	3	3	1
Glass syringe barrel - heat	3	4	1	3	2
Glass syringe barrel washing	3	4	3	3	1
Glass syringe barrel sterilization and siliconization - heat	3	4	1	3	2
Glass syringe barrel sterilization and siliconization – heat – DI water	3	4	3	3	1
Glass syringe barrel sterilization and siliconization – heat – ethylene oxide	3	4	3	3	1
Glass syringe barrel sterilization and siliconization – heat – silicone	3	4	3	3	1
Staked needle	1	2	3	2	3
Needle Cover (rubber tip cover)	1	2	3	2	3
Needle Cover (rigid cover)	1	2	3	2	3
Syringe plunger rod	1	2	3	2	3
Syringe plunger stopper	1	2	3	2	3

Process	Reliability	Complete-ness	Temporal Correlation	Geographical Correlation	Technological Correlation
Syringe plunger stopper sterilization - heat	3	4	1	3	2
Syringe plunger stopper sterilization - water	3	4	3	3	1
Assembly energy	3	4	1	3	2
Drug	3	1	1	1	3
Packaging PFS - PVC	1	1	3	2	2
Packaging PFS - paper	1	1	3	2	2
Packaging tertiary	3	1	3	2	2
Packaging pallet	3	1	3	2	2
Distribution	3	1	3	2	1
Landfill disposal	1	1	3	2	1

Table C6. Data Quality Indicator system of the Pedigree Matrix

DQI	Description	Value
Reliability	Verified data based on measurements	1
	Verified data based on assumptions or non-verified data based on measurements	2
	Non-verified data partly based on qualified estimates	3
	Qualified estimate (e.g., by industrial expert)	4
	Non-qualified estimate	5
Completeness	Representative data from all sites relevant for the market considered, over an adequate period to even out normal fluctuations	1
	Representative data from >50% of the sites relevant for the market considered, over an adequate period to even out normal fluctuations	2
	Representative data from only some sites (<<50%) relevant for the market considered or >50% of sites but from shorter periods	3
	Representative data from only one site relevant for the market considered or some sites but from shorter periods	4
	Representative unknown or data from a small number of sites and from shorter periods	5
Temporal Correlation	Less than 3 years of difference to the time period of the dataset	1
	Less than 6 years of difference to the time period of the dataset	2
	Less than 10 years of difference to the time period of the dataset	3
	Less than 15 years of difference to the time period of the dataset	4
	Age of data unknown or more than 15 years of difference to the time period of the dataset	5
Geographic Correlation	Data from area under study	1
	Average data from larger area under study is included	2
	Data from area with similar production conditions	3
	Data from area with slightly similar production conditions	4
	Data from unknown or distinctly different area (North America instead of Middle East, OECD-Europe instead of Russia)	5
Further Technological Correlation	Data from enterprises, processes and materials under study	1
	Data from processes and materials under study (i.e. Identical technology) but from different enterprises	2
	Data from processes and materials under study but from different technology	3
	Data on related processes or materials	4
	Data on related processes on laboratory scale or from different technology	5

APPENDIX D: Critical Review Statement

Harmony Environmental, LLC
Management • Analysis • Communication
Beyond Sustainability, Striving for Harmony

Critical Review Statement

Date: May 31, 2024

LCA Commissioned by: ApiJect Systems, Corp

LCA Conducted by: Dr. Matthew Eckelman, environmental engineer and LCA practitioner, and Dr. Robert Litan, economist

Report Title: Life Cycle Assessment of the ApiJect Prefilled Injector (May 17, 2024)

Review Conducted by: Terrie Boguski, Harmony Environmental, LLC (Chair)
Cassandra Thiel, New York University
C. Jason Pierce, LCA Consultant and Certified Practitioner

ISO Referenced Standards: ISO 14040:2006; ISO 14044:2006+Amd1:2017+Amd2:2020; ISO/TS 14071:2014

Critical Review Process, Scope and Conclusion

In accordance with the international standard, ISO 14044:2006, a Critical Review was conducted by an external, independent review panel of the life cycle assessment (LCA) report, *Life Cycle Assessment of the ApiJect Prefilled Injector*. The cradle-to-grave LCA compares the environmental impacts of several options for injecting sterile liquid medicines into patients. This was an end-of-report review, and reviewers received the entire LCA report. The review was based on the stipulations in ISO 14044:2006. The review followed guidance in ISO 14071:2014.

The reviewers received the LCA report on April 10, 2024 and provided first-round review comments to the LCA practitioners on April 29, 2023. The reviewers received the revised report on May 17, 2024 and verified that the report conforms to ISO 14044 on May 31, 2024. The review was conducted by exchanging comments and responses via email. Comments were logged in an Excel spreadsheet based on Annex A of ISO/TS 14071:2014. These are appended to the critical review statement.

The reviewers checked that the LCA report followed the stipulations set forth in the ISO 14040 and 14044 standards, including the following aspects:

- principles and framework;
- goal and scope definition;
- inventory analysis;

- life cycle environmental impact assessment; and
- interpretation of results.

The findings of the reviewers concluded that all required stipulations in ISO 14044:2006 6.3 were met in the revisions to the report (received May 17, 2024). In particular,

- The methods used to carry out the LCA are consistent with this International Standard,
- The methods used to carry out the LCA are scientifically and technically valid,
- The data used are appropriate and reasonable in relation to the goal of the study,
- The interpretations reflect the limitations identified and the goal of the study, and
- The study report is transparent and consistent.

The reviewers did not review other underlying data, life cycle inventory (LCI) calculations or LCA models. Therefore, the review is limited to the summary LCI data and LCA model results included in the report.

Participation in the critical review does not mean the reviewers endorse the results of the LCA study, nor does it mean that they endorse the assessed products.

ISO 14044:2006 requires that this critical review statement, as well as the reviewers' comments and any responses to recommendations made by the reviewers be included in the final LCA report.

Submitted on behalf of the review panel members by:

Terrie Boguski

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