1. Purpose & Scope

The purpose of this position paper is to document the collaborative project between Zipline and Pfizer that was initiated to develop an end-to-end process for shipment of Ultra Low Temperature (ULT) vaccines (-90° to -60°C) from Pfizer in Puurs, Belgium to Zipline Distribution Centers in Ghana and to the final Points of Use (POUs) within Ghana at 2° to 8°C. This end-to-end process was in alignment with the Deconsolidation and Redistribution of Pfizer & BioNTech's COVID-19 Vaccine. The last mile delivery was selected as 2° to 8°C for this project based on the acceptability to transport the vaccines at this temperature range. Below are the key areas for the end-to-end process:

- Development of secondary packaging systems to contain vials for last mile delivery when transported with Zipline UAS Aircraft.
- Qualification of tertiary (thermal) packaging for the last mile delivery from Zipline Ghana to POUs within Ghana to maintain temperatures of 2° to 8°C, which is an acceptable temperature after deconsolidation, against worst case Summer and Winter profiles. This aligns with the Deconsolidation and Redistribution of Pfizer & BioNTech's COVID-19 Vaccine, where transport must be less than or equal to 12 hours at this specified temperature. Note: Pfizer & BioNTech's COVID-19 Vaccine can be stored and transported at -90° to -60°C for up to 9 months (current stability data), however for last mile delivery there is the option to store and transport at 2° to 8°C for up to 1 month.
- Qualification of ULT Freezers for receipt and storage of ULT vaccines.
- Distribution Testing Technical Report analyzing shock and vibration data based on Zipline's UAS Aircraft Mode of Transport and comparing it against the distribution simulation data profiles performed previously on the Pfizer & BioNTech's COVID-19 Vaccine. This would then deem equivalency to the product quality testing that was already performed on Pfizer & BioNTech's COVID-19 Vaccine.
- Distribution Testing on the thermal packaging with phase change material (PCM) to evaluate any damage to the PCM during delivery and to ensure the system can maintain appropriate temperatures during delivery.
- End-to-End Testing (Performance Qualification) with the following process flow:
    - Shipment of simulated vaccine (placebo) from Pfizer in Puurs, Belgium to Zipline Ghana using Pfizer's qualified ULT thermal shipping container for maintaining temperatures of -90° to -60°C using a representative transportation Carrier.
    - Receipt of placebo into the two most remote Zipline Distribution Centers in Ghana and storage in qualified ULT freezers capable of maintaining -90° to -60°C, which is one of the acceptable storage conditions for WHO countries.
    - Conditioning of placebo at 2° to 8°C before pack-out into Zipline's qualified thermal packaging with PCM.
    - Pack-out and shipment within Zipline's qualified thermal packaging with PCM, delivering by Zipline's UAS Aircraft to four representative POUs, two from GH3 and two from GH4 distribution centers. This testing only included the Summer Pack-Out based on the ambient temperature in Ghana.
    - Results from the last mile delivery for temperature assurance and visual inspection of secondary packaging and vials.

This position paper will not encompass:

- Use of data from simulated shipping studies with post quality attribute testing for other Manufacturers' vaccines without appropriate testing.
- Post receipt and processing activities directly at the POU.
- Analysis of the Zipline Quality Management System.

2. Background

Pfizer and Zipline share a common strategic goal: A commitment to work towards equitable access for COVID-19 vaccines for people around the world, especially in the hardest to reach areas.

Despite a global trend toward urbanization – in Asia and Africa in particular – many people still live in rural areas that are difficult to access due to underdeveloped infrastructure and insufficient transportation capabilities.

Pfizer and Zipline recognized an opportunity to leverage their existing partnership to create a scalable and robust process that allows for COVID-19 vaccines to be distributed to remote locations globally. Therefore, testing was designed for the end-to-end supply chain, from a vaccine manufacturing facility in Europe to last-mile health posts in rural Ghana, to illuminate requirements to move product efficiently, quickly, and with the highest quality control.

3. Discussion of Data

3.1. Secondary Packaging Development

There were three goals when developing the secondary packaging to transport the COVID-19 vaccine vials for last mile delivery.

- Protect the vaccine vials in last mile delivery via Zipline's UAS aircraft.
- Allow for variability in the number of vials sent within each shipment.
- Design a secondary package that will integrate with the Zipline UAS last-mile delivery thermal packaging solution.

The Zipline Engineering team worked with a US-based manufacturing company on the design and development of secondary packaging with the three goals in mind. Throughout the development process, special coordination with Zipline's Thermal Packaging Supplier was required to design secondary packaging that would successfully integrate with the UAS last-mile delivery thermal packaging.

The design allows for a minimum delivery of one vial of the vaccine and a maximum delivery of 25 vials, sized for a 2 ml vial. In addition, the secondary packaging design includes a partition within the carton to allow a cell for the variance in order quantities. Another attribute that was built into the partition was an air cell on the edges as extra protection to the vials.

3.2. Qualification of thermal packaging with PCM for Last Mile Delivery at 2° to 8°C

The initial goal of the thermal packaging workstream was to design a solution that fit within the existing Zipline outer corrugated shipper, which includes a bubble cushion (protection packaging) and parachute. The acceptance criteria for the thermal packaging solution were to maintain temperatures of 2° to 8°C for a minimum of 4 hours for the last mile delivery UAS Aircraft flight. This duration exceeds required flight times, but accounts for unplanned events resulting in drones being rerouted back to the Zipline Distribution Center. The second goal was to ensure that all thermal packaging development and associated qualifications adhere to GxP requirements.

Zipline's Packaging Supplier in the US was used for the design and qualification of the thermal packaging. The overall qualification process for Zipline's Packaging Supplier included both Design Qualification and Operational Qualification Testing. The Design Qualification Testing was to demonstrate that the thermal packaging was suitable for intended purpose, including environmental chamber testing to test the pack-out and test profiles with confidence before going into the Operational Qualification Testing. The goal of the Operational Qualification is to demonstrate the limits of the thermal packaging against the test profiles (i.e., Summer and Winter) and to verify the configuration with appropriate PCM in the thermal packaging, time, and temperature ranges for the thermal packaging and practical pack-out steps to maintain the required internal temperatures. The Distribution Testing and Performance Qualification are documented in subsequent sections of this position paper.

The temperature profile design requirements were based on global distribution requirements using +43°C Summer Soak as worst case leveraged from a version of the WHO Guidelines and the Winter Soak profile was set to 0°C since the Zipline UAS aircraft don't currently fly in temperatures below 0°C.

There was also a request to design a pack-out that was universal for Summer and Winter to avoid operational complexities for use. However, the Packaging Supplier ended up developing a Seasonal Conditioning pack-out for Summer and Winter. Summer Phase Change Material (PCM) conditioning included refrigerated (5° ± 3°C) for two PCMs closest to payload and one frozen PCM (-24° ± 3°C) around the refrigerated PCM. Winter PCM conditioning included refrigerated (5° ± 3°C) conditioning for both models of PCM. During the design phase of the thermal

packaging, the Packaging Supplier determined that insulation would be required in addition to the PCM to meet the soak profiles (+43°C, 4 hours and 0°C, 4 hours).

The Design qualification (DQ) was performed by the Packaging Supplier in an environmental chamber including the insulation around the PCM. During this phase it was determined that in addition to insulation around the PCM, rubber bands would be needed to better secure the PCM to the payload without gaps. The rubber bands were suggested as an output from the DQ where, during the Summer Profile, the duration was slightly less than 4 hours between 2° to 8°C.

The Packaging Supplier executed Operational Qualification testing in an environmental chamber with results that met the acceptance criteria of 2° to 8°C for a minimum of 4 hours. The OQ encompassed minimum load/maximum volume triplicate testing against +43°C and 0°C profiles. Minimum load is an empty payload, but maximum volume as worst case. Five probes representing simulated product locations within the empty payload were used and 1 air probe for each sample tested (3 air probes) per profile. The air probes are the locations outside of the thermal packaging measuring the environmental chamber temperatures.

The high-level results are indicated below:

- Summer Profile Testing (+43°C) met a minimum duration of 4 hours and 22 mins with temperatures between 2° to 8°C.
- Winter Profile Testing (0°C) met a minimum duration of 4 hours and 59 mins with temperatures between 2° to 8°C.

Based on the testing, the Packaging Supplier indicated that the Summer Conditioning Pack-Out would be executed for temperatures at or above 10°C and the Winter Conditioning Pack-Out would be executed at or below 9°C.

There was a request to the Packaging Supplier to perform some additional testing at the temperature cut-offs between the two different conditioning temperatures for the PCM pack-outs based on the results from the end-to-end testing. The results are indicated below.

- Summer Pack-Out, tested at (+10°C) and lasted 5 hours and 31 mins with temperatures between 2° to 8°C.
- Winter Pack-Out, tested at (+9°C) and lasted 6 hours with temperatures between 2° to 8°C.

Results indicated that the system maintained controlled temperatures of 2°C to 8°C for 4 hours against the recommended lowest temperature for Standard Summer Pack-Out (ambient profile of constant 10°C) and the recommended top temperature for the Winter Pack-Out (ambient profile of constant 9°C).

3.3 Qualification of ULT Freezers

The Zipline Distribution Centers in Ghana are equipped with Stirling Ultra-Low Storage Freezers – model SU780XLE.

These units were purchased at a time when there was significant demand for ULT freezers to support upcoming vaccine distribution. The lead time for receiving the units was 6-8 weeks in the case of Zipline's most remote Distribution Centers.

After receiving the ULT freezers at each Distribution Center, Zipline contacted Ghana Standards Authority (GSA) to assist with the qualification of the ULT freezers. GSA has a single person on staff that qualifies these types of units. This person was booked out for 5-6 weeks. The GSA recommended the appropriate probes and equipment needed to qualify the freezers to the Zipline Quality Team. Zipline was able to obtain the required probes and equipment in 3 weeks and qualified the Stirling ULT freezers, following the process and requirements published by Stirling and GSA.

At a high level, the qualification entailed using the Installation and Operational Qualification Validation Package from Stirling. The installation qualification entailed confirming appropriate installation based on the Manufacturer's recommendation. Within the operational qualification, the functions of the ULT freezer were tested, including the alarms. A 24-hour mapping was performed on a full and empty ULT freezer as part of the operational qualification. In both scenarios, the ULT freezers also went through a power failure test, including time to recover and an open-door time to recover test.

3.3. Distribution Testing Technical Report Analyzing Shock & Vibration Zipline Profile Against Industry Tested Profile for Pfizer & BioNTech's COVID-19 Vaccine (Product Quality Testing)

To determine if the Pfizer COVID-19 vaccine would meet product quality attribute requirements during Zipline's UAS aircraft delivery, distribution testing comparisons in terms of shock and vibration were assessed. Tests were designed to determine if Zipline's delivery environment fell within what had been previously tested through simulation on the Pfizer COVID-19 vaccine that included post product quality attribute testing.

A technical assessment was generated to analyze the shock and vibration exposures during Zipline UAS aircraft delivery. The comparison was made between the Zipline UAS aircraft delivery shock and vibration profiles to the profiles that Pfizer had previously tested for the COVID-19 vaccine. It was determined that Zipline's UAS vibration environment is milder than steel spring trucks and the expected shock exposures are milder than what was tested in the product transportation simulation study.

Within this same technical assessment, data was used from an engineering study that was executed to collect shock data in a laboratory, for Zipline's UAS aircraft delivery solution when exposed to shock events expected during delivery. The shock events indicated that the peak acceleration during impact upon landing using the Zipline drone delivery thermal packaging with a terminal velocity of 8 m/s is 156-162 G for both the Summer and Winter Pack-Outs. The peak acceleration by the product vials during drop testing from a 36-inch drop averaged 194 G for thawed/refrigerated product with a weight of 10.4 lbs. This is comparable to the Zipline thermal packaging requirement of 2° to 8°C. When comparing a dry ice thermal packaging configuration with product vials and a drop height of 36 inches, this came out to 428 G.

Since the shock and vibration testing for the drone delivery is milder than that tested by Pfizer, including product quality attributes it can be concluded that the existing data for product quality attributes are valid for drone delivery.

3.4. Distribution Testing on Thermal Packaging with PCM

A physical Operational Qualification (OQ) study was executed in a laboratory on the Zipline UAS Aircraft Delivery thermal solution to test whether it can withstand the physical challenges of UAS Aircraft delivery. The sample size included replicate samples of the Summer Pack-Out PCM pack-out and Winter Pack-Out PCM pack-out.

Physical qualifications of thermal packaging are part of shipping validation to ensure the package is robust to distribution hazards. This study was executed per a modified ISTA 3A, Standard Test Procedure for Laboratory Simulated Test Sequences for the Performance of Parcel Packaging within the Distribution Environment. A modified testing sequence was used to expose the packaging system to the expected transport hazards for Zipline UAS aircraft delivery.

The vibration testing sequences were completed without any top loading as the thermal packaging system for the drone delivery does not include the potential for stacking. Testing was completed with Face 3 down since that is the orientation of the thermal packaging in the drone for delivery. Random vibration (over-the-road) was completed for 120 mins and Random vibration (pick-up and delivery) was completed for 30 mins.

The drop sequence was modified for drone delivery, which included two bottom face drops, one drop onto two opposite bottom corners, and four face drops. The eight drops exceed the one shock event likely to be encountered for each drone delivery with a parachute deployed during this drop.

The testing included temperature monitoring during distribution testing and inspections of the primary/secondary packaging for informational purposes. The main acceptance criteria in this testing was the condition of the thermal packaging. Testing was conducted using maximum payload to ensure worst case was tested.

The results post testing indicated that the vials were not broken, and labels, secondary packaging, outer packaging, and bubble cushioning remained intact. Labels remained legible. From the thermal packaging perspective, no leaks were observed on the PCM and the insulation also had no major damage. There was a minor low temperature excursion noted in the Summer Pack-Out during distribution testing, although supported by stability data.

3.5. End to End Testing (Performance Qualification)

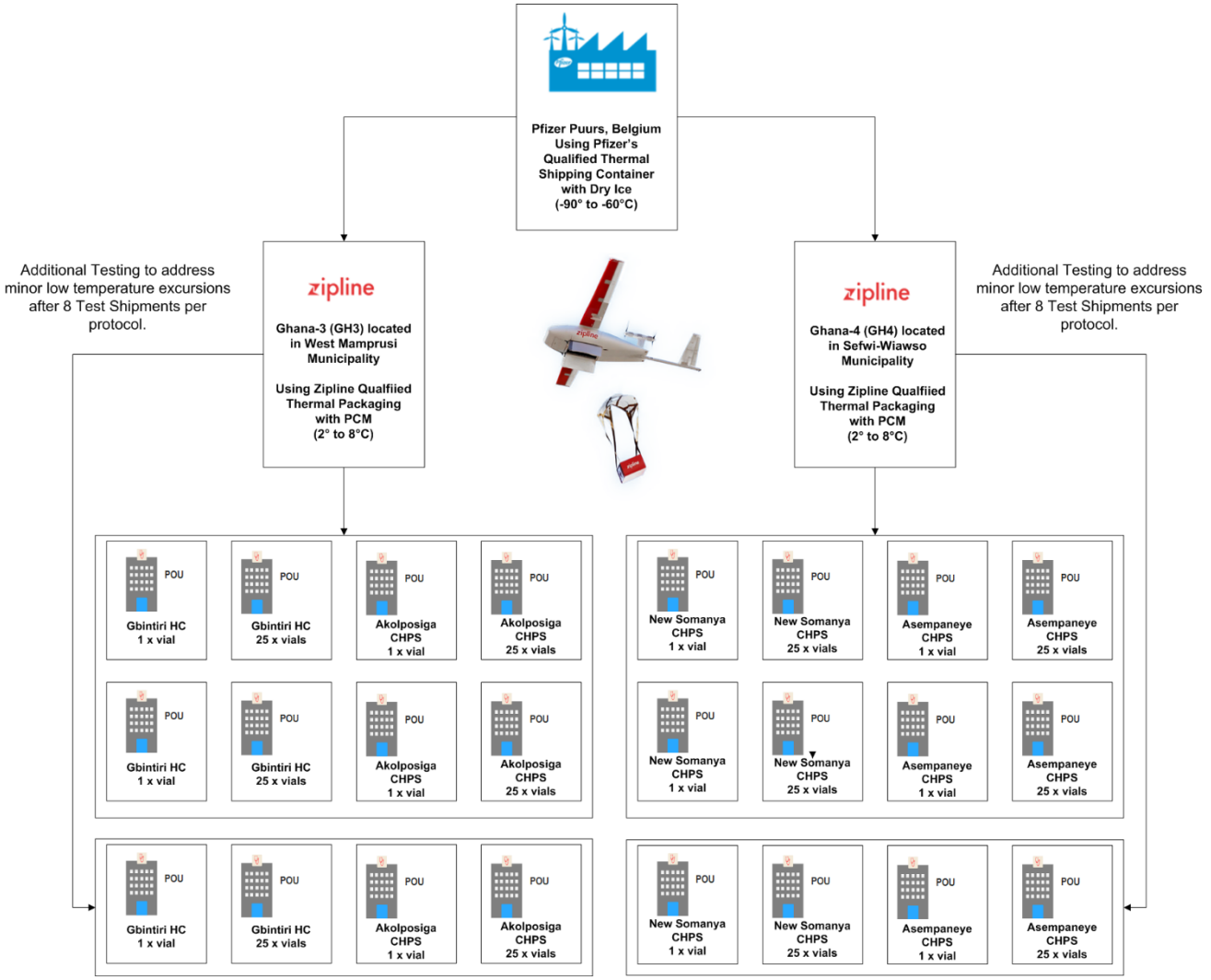
The goal of the end-to-end transportation testing (Performance Qualification) was to ensure that the placebo vials (water filled vials), as representative of Pfizer & BioNTech's COVID-19 vaccines, maintained appropriate temperatures and remained intact and safe throughout each delivery leg. This testing also incorporated verifying that the last mile delivery thermal packaging from Ghana to POU operated as intended as per the OQ. The first leg of the shipments was executed from the manufacturing site of the vaccine in Belgium to two of Zipline Ghana's Distribution Centers, Ghana-3 (GH3) located in West Mamprusi Municipality and Ghana-4 (GH4) located in Sefwi-Wiawso Municipality. The shipments for this first leg from Belgium to Zipline Distribution Centers used Pfizer's qualified thermal shipping container with dry ice for maintaining temperatures of -90° to -60°C during transportation. GH3 and GH4 are the furthest Zipline Distribution Centers from the entry port in Accra, Ghana, and were chosen to highlight the most extreme and remote transportation scenario for testing. Similarly, the most remote final points of use locations were used for final delivery from the Zipline Distribution Centers. This included Gbintiri Health Center and Akolposiga CHPS (health post) as POUs originating from GH3 and New Somanya CHPS (health post) and Asempaney CHPS (health post) as POUs originating from GH4.

The end-to-end testing also included confirmation of the processes that were put in place at Zipline for:

- Receipt of the placebo
- Storage into qualified ULT Freezers
- Conditioning of the placebo at 2° to 8°C for thawing prior to deconsolidation into secondary packaging
- Conditioning of the PCM for Summer thermal packaging pack-out
- Deconsolidation of the placebo into secondary packaging (minimum configuration 1 and maximum configuration 25)
- Final pack-out into thermal packaging for delivery to the POU

At both GH3 and GH4, the thermal shipping containers with the placebos were received successfully and the placebos were immediately stored in Zipline's qualified ULT Freezers per their local standard operating procedures. Zipline followed the requirement to store the placebos in a 2° to 8°C environment for thawing prior to deconsolidation into their secondary packaging for a minimum of 3 hours as per the Deconsolidation and Redistribution of Pfizer & BioNTech's COVID-19 Vaccine. No major issues were reported for these two processes.

Below is the high-level flow chart of the shipments that were executed under protocol from Zipline Ghana Distribution Centers, GH3 and GH4 to POU.



Eight shipments were executed from GH3 to two different POUs and eight shipments were executed out of GH4 to two different POUs using thermal packaging for last mile delivery targeted to maintain 2° to 8°C. Replicate testing of minimum loads (1 vial) and maximum loads (25 vials) were executed to the two different POUs from GH3 and GH4. The results from these shipments indicated that the Zipline thermal packaging met visual inspection requirements. In addition, all vials remained intact and not broken and the secondary packaging and simulated tamper evident label remained intact.

From a temperature perspective, there were some minor low temperature excursions that occurred below 2°C, but above 1°C. Although the minor excursions were supported by stability data, Zipline's investigation determined that the set temperature of their freezers for the conditioning of the frozen PCM were lower than the manufacturer's recommended specification. Furthermore, the Packaging Supplier also performed parallel path fringe testing for the cut-offs between the two seasonal conditioning requirements for the PCM pack-outs as extra data. A summary of this testing is specified in Section 1.2, Qualification of thermal packaging with PCM for Last Mile Delivery at 2° to 8°C of this position paper.

There were also some minor high temperature excursions above 8°C at the beginning of the temperature monitoring period. The standard start-up delay for Temperature Measuring Devices used by Zipline is 5 mins and pack-out into secondary packaging occurs at room temperature (i.e., 15° to 25°C), which is acceptable per the Redistribution Considerations for Pfizer & BioNTech's COVID-19 Vaccine. There is an acclimation period with the PCMs, but a minimum start-up should be used since the flight time during the last mile delivery is typically closer to 1 hour, but

some durations were up to 3 hours. Zipline uses temperature monitoring requirements for last mile delivery to align with local Board of Health requirements.

Additional last mile delivery test shipments were executed after Zipline implemented the appropriate set temperature for their freezers used to condition the frozen PCM. This included two minimum configurations (1 vial) and two maximum configurations (25 vials) executed out of GH3 and GH4 to POUs. Testing met requirements with some additional actions for Zipline to update work instructions for the correct pack-out of PCM (5 ± 3°C), so they are interlocking C's around the payload to avoid air gaps.

In conclusion, Zipline's storage capabilities, handling processes, and thermal packaging were found to ensure adequate delivery of the vaccine to health facilities. Throughout the end-to-end testing, opportunities and challenges are highlighted in the conclusion to share learning with others on how to best prepare for distribution with multiple temperature requirements on various legs, leg 1 (-90°C to -60°C) and leg 2 (2° to 8°C).

4. Conclusion

The data in this position paper summarizes the following five key workstreams focused on during the partnership between Zipline and Pfizer to create the scalable and robust process that allows for COVID-19 vaccines to be distributed to remote locations initially tested for Ghana and potentially for global expansion. At a high level, below are the key learnings summarized by the workstreams.

Workstream	**Learnings**
Secondary Packaging Development	● Variability in the amount of vaccine delivered was an important goal in the secondary packaging design. ● Feedback from government partners in Ghana indicated demand is unpredictable across the country. The ability for Zipline to send only the number of needed doses on demand helps ensure safe storage guidelines are upheld and no vaccine is wasted.
OQ Testing of Thermal Packaging with PCM for Last Mile Delivery at (2° to 8°C)	● PCM alone did not maintain 2° to 8°C for extreme temperature profiles. This was exemplified by the design work performed by the Packaging Supplier and additional insulation added to the design. ● A consistent pack-out of PCM is required to prevent air from traveling to the payload area when using a mixture of conditioning temperatures (i.e. 5° ± 3°C and -24° ± 3°C) for the PCM. ● A universal thermal pack-out for all seasons is a first choice to avoid operational complexities with different conditioning requirements based on the temperatures in a region and season. Although it was understood with extreme temperature profiles and minimal space this can be challenging. ● When working as tripartite organizations it is important that requirements are documented up front for clear and efficient execution.
Qualification of ULT Freezers	● Demand for ULT freezers remains high. The sooner a country can create a distribution strategy, determine the number of units needed, and order those units, the lower the chance of delays in receiving vaccine. ● Resources for qualification can be very limited. Stirling and other manufacturers have validation packages that can be

	procured for installation and operational qualification requirements. Countries should include a qualification plan as part of their overall distribution strategy and timeline.
Distribution Testing Technical Report – Deem equivalency to testing that was already performed by Pfizer for product quality testing	● During shock event comparisons, it is critical to include similar temperature profiles to ensure accurate analysis.
Distribution Testing on Thermal Packaging with PCM for Last Mile Delivery	● There is no recognized standard that exists for drone mode of transport for distribution testing. Therefore, educated assumptions were made to determine appropriate vibration and impact testing requirements leveraging the industry standards as a baseline for the drone profile.
End to End Performance Qualification from Mfg. to POU in Ghana	● Transportation from Origin to port (Accra) in Ghana: o There should be an agreement on strategy for door to door transport vs. door to port. o Carriers should deliver vaccine when released from customs vs. waiting for other shipments to release to reduce delays, as the Pfizer-validated thermal shippers are designed to maintain -90°C to -60°C for a maximum of 10 days without re-icing. o Carriers should ensure shipments are identified with separate MAWB associated with HAWB. o Carriers should perform In-Transit Re-Icing based on calendar for excessive time in customs. ● Thermal Pack-Out for Last Mile Delivery: o Correct conditioning of the PCM as -24 ± 3°C is critical to alleviate low temperature excursions. (This has been addressed by Zipline.) o Correct pack-out of PCM (5 ± 3°C), so they are interlocking C's around the payload, avoids air gaps. (This is being addressed by updates to FUL-WI-002 for pack-out with better pictures and retraining of staff that pack-out the solution.) ● Temperature Monitoring: o Temperature monitoring for last mile delivery to align with local Board of Health requirements.

5. References

Document ID Within Paper	Title
OPS23M21POZDP	Qualification Report for Zipline Drone Pharma Pack-out for Shipping Product between 2°C and 8°C for 4 Hours Note: Cross reference to Design Qualification Report is specified in this document.
N/A (Stored in Zipline's Document Management System)	Operational Qualification Fringe Temperature Tests Testing the cut-off temperatures for switching between Summer and Winter Pack-Outs

ZIP-RPT-30AUG2021	Report for Physical Qualification of BioPCM Zipline Drone Delivery Solution (Pharma Pack-out for 2-8°C)
ZIP-RPT-21JUN2021	Technical Report for Evaluation of Drone Distribution Shock and Vibration for Zipline
PR-ZIPL-01	Protocol, Thermal Performance Qualification Transportation of Ultra Low Temperature Vaccines From Point of Origin to Service Delivery Point
FUL-TESTREP-001	Report, Thermal Performance Qualification Transportation of Ultra Low Temperature Vaccines From Point of Origin to Service Delivery Point
FUL-SOP-088	Global Fulfillment SOP - Receipt and Storage of Pfizer-BioNTech COVID-19 Vaccines
FUL-TR-002	Pfizer Testing Process Instructions and Training Document
09633-000	Package Air Insert
09678-000	Outer Box
21-0321-4010	Vaccine Vial Box Outer Box
21-0321-405	Vaccine Vial Box Inserts
16210Z0579-JAG	Flexmat Q1 Bio PCM
16210200540-JAG	Pouch Q5 Bio PCM
FUL-WI-002	Pfizer Cold Chain Package Work Instruction

6. Appendices

N/A

7. Change History

Issue Number	Description of Change(s)	Reason for Change(s)
1.0	Initial Release	Initial Release