FROM SKY TO SHAKER: A CASE STUDY ON REPLICATING DRONE-INDUCED VIBRATION FOR THE ASSESSMENT OF THE INTEGRITY OF MEDICAL PRODUCTS

K Theobald University of Southampton, Southampton, United Kingdom
T Waters University of Southampton, Southampton, United Kingdom
T Cherrett University of Southampton, Southampton, United Kingdom

1 INTRODUCTION

One of the key anticipated applications for drone delivery is for medical products, replacing traditional types of ground transport such as vans and lorries. This is an area with ever increasing news coverage, as well as academic publications and operational trials[1]. This use case often focuses on the delivery of pathology samples as well as blood products and other routine and emergency medicine. Arguably the most successful operation, to date, is that conducted by Zipline who have been operating across central Africa since 2016[2]. Making over 1 million deliveries globally and covering over 70 million miles[3].

By contrast, drone delivery for medical applications has not progressed beyond trial stages in the UK, although several pilot projects have explored its potential. Apian, in collaboration with Skyports, conducted trials transporting medical products between hospitals in northern England with further trial expected in Autumn 2024[4]. Windracers has undertaken flight tests of its fixed-wing drone for medical deliveries in the Isle of Wight[5] and the Isles of Scilly[5, 6]. Additionally, Skyports has partnered with Swoop Aero to trial a vertical take-off and landing (VTOL) drone for transporting COVID-19 medical supplies in Scotland[7]. However, none of these have developed into full services to date.

The progression of drone-based medical logistics from experimental trials to routine operations has been hindered in the UK by stringent airspace regulations. Currently, drone flights beyond visual line of sight (BVLOS) are restricted to designated Temporary Danger Areas (TDAs), impeding widespread or repeated implementation. Additionally, the pharmaceutical industry faces challenges in demonstrating the consistent quality and safety of medical products during drone transportation. Regulatory bodies, such as the UK Medicines & Healthcare Regulatory Agency (MHRA), demand rigorous evidence that the transportation process does not compromise product integrity. They have established stringent guidelines for the transportation and storage of medicines, emphasising the importance of multi-layer packaging and precise temperature control. However, the impact of vibration on medical cargo during transportation, particularly by drones, remains largely unexplored. Previous studies have identified significant vibration levels in a variety of drones[6, 8, 9], raising concerns about potential damage to costly sensitive medications such as monoclonal antibodies (mAbs) used in the treatment of cancer.

MAbs are thought to be particularly vulnerable to vibration due to their protein-based structure, which can be disrupted by physical stressors resulting in aggregation or fragmentation leading to a loss of efficacy. While some research has examined the effects of shaking and stirring on mAbs[10], these conditions do not accurately replicate the complex vibration patterns experienced during drone flight. Limited studies involving drone transportation of mAbs have shown encouraging results, reporting no significant impact on medication quality[6, 8, 9]. However, these studies have typically involved short flight durations and simple flight paths, limiting their ability to assess the long-term effects of vibration on medication integrity.

The ability to test the stability of medicines during live flight trials is currently severely limited due to expense, safety risks and required permissions. This study develops and tests a framework for assessing the integrity of medicines intended for drone transport using a vibration shaker to replicate measured flight data.

1.1 Background Guidance and regulation

The Civil Aviation Authority (CAA) provides all relevant policy and guidance for the operation of drones in the UK. This includes guidance for payloads classified as dangerous goods which must also be packed in accordance with UN3773[11] and PI 650[12], for example blood and other pathology samples. In the case of dangerous goods it may also be necessary to utilise a crash-proof container. The requirements of a crash-proof container are set out by the Vehicle Certification Agency (VCA) procedure, crash-protected containers for dangerous goods carried by remotely piloted aircraft systems[13] while their application is dictated by the CAA CAP2555[14].

The transportation of medicines governed by stringent regulations to ensure product quality and patient safety such as the European Union Good Distribution Practice (GDP) Guide-lines[15] and the UK Medicines and Healthcare Regulatory Agency (MHRA) Green Guide[16]. Where medicines lack clear classification as hazardous materials or in the case of non-typical transportation such as delivery by drone, a case by case assessment is required in which evidence of stability during and after transport may be required.

1.2 Vibration testing standards.

Vibration testing for the performance of packaging used in ground transportation is generally well established. In most methodologies vibration tests are used to simulate vibrations typically experienced during transportation and visually inspected to determine whether the contents of the packaging have been adversely affected during transit. There are several methodologies to undertake this of which the most common form of test is a single-level test. For this, a random broadband vibration is excited in a single direction. Examples of this test include ISO 13355[17], ASTM D4169[18], D4728[19] and GB/T 4857.23[20]. In these methodologies the random signal is generated to contain all frequencies within a defined range or to suit a predefined power spectral density (PSD). Within these standards the limits and PSDs are specified to focus only on vibration experienced during road transport which tends to be lower frequency than those experienced during drone flight. Tests can either be undertaken in real-time to match real-life transport durations or can utilise time compression in which an increase in intensity is used to compensate for a reduction in test duration. The primary criticism of single-level, time compressed tests is that the vibration in the trial does not correlate well with the target environment and therefore may not be appropriate for sensitive products. This is arguably even more significant in the context of medical goods as it is not clearly understood if the relationship between duration and intensity holds true for aggregation fragmentation as modes of failure.

1.3 Vibration Replication Trials

In the literature there have been several laboratory-based trials to simulate transport vibration profiles during road transport. Zheng et al.[21] simulated transport vibration profiles using a laboratory set up comprising an electrodynamic shaker, an amplifier, data acquisition, control system and accelerometers. The road spectrum used was that of a composite truck spectrum described in ASTM D4169[18]. This set up allowed the controlled testing of other variables such as packaging arrangement.

Replication of vibration profiles for drone transportation has been undertaken by Johannessen et al.[22]. This trial subjected blood samples to simulated high turbulence flight. A 'high force' electrodynamic shaker was utilised to subject the samples to random vibration over a 5Hz-200Hz frequency range. Samples were split between 1 hour and 2 hour flights with 25 and 50 episodes of turbulence respectively. Episodes of turbulence had peak acceleration between 10 and 30g acceleration. The blood showed little vulnerability to the vibration they were exposed to. This trial showed the effectiveness of a bench trial to test the consequences of drone flight on medical samples.

2 OUTLINE EXPERIMENTAL STRUCTURE

The proposed methodology for drone flight vibration replication consists of three key stages as indicated in the schematic in Figure 1: (i) vibration recordings of real drone flights are taken, (ii) recordings are processed and analysed, and (iii) the processed recordings are replicated through an electrodynamic shaker.

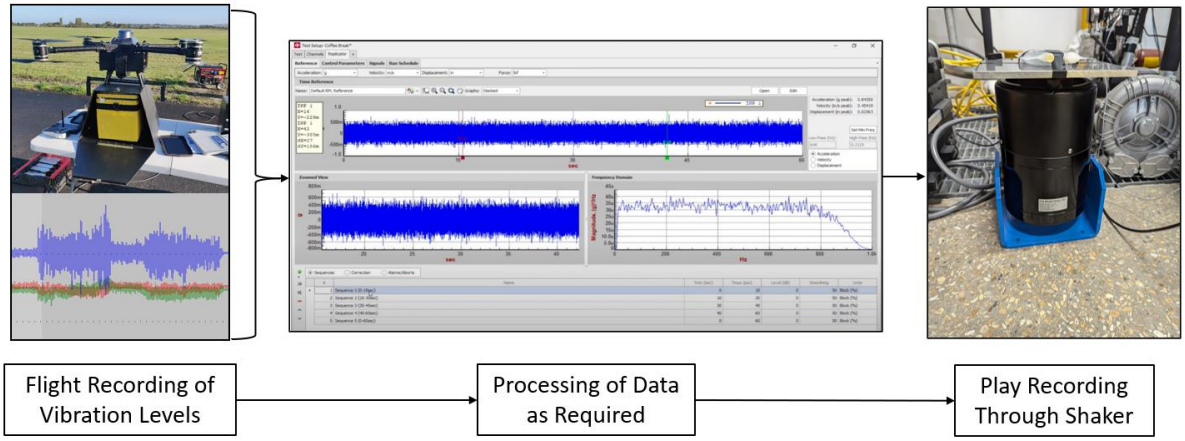


Figure 1: Schematic diagram of the experimental process.

The following sections provide further details of each of these stages.

3 DRONE FLIGHT RECORDING

3.1 Drone Platform

The drone platform used in this example test was the Soton UAV Spotter drone. This is a fixed wing drone platform (Figure 2.) powered by twin, single cylinder, four-stroke petrol engines with an operating speed between 3,000-8000 RPM. This platform has a 4m wingspan with a maximum payload capacity of 5 kg.

The example flight was undertaken at Draycot Farm Aerodrome GB-0006. A single flight taking 43 minutes was undertaken following both clockwise and anticlockwise circuits at constant altitude of 110m covering a distance of approximately 17km.

(a) (b)

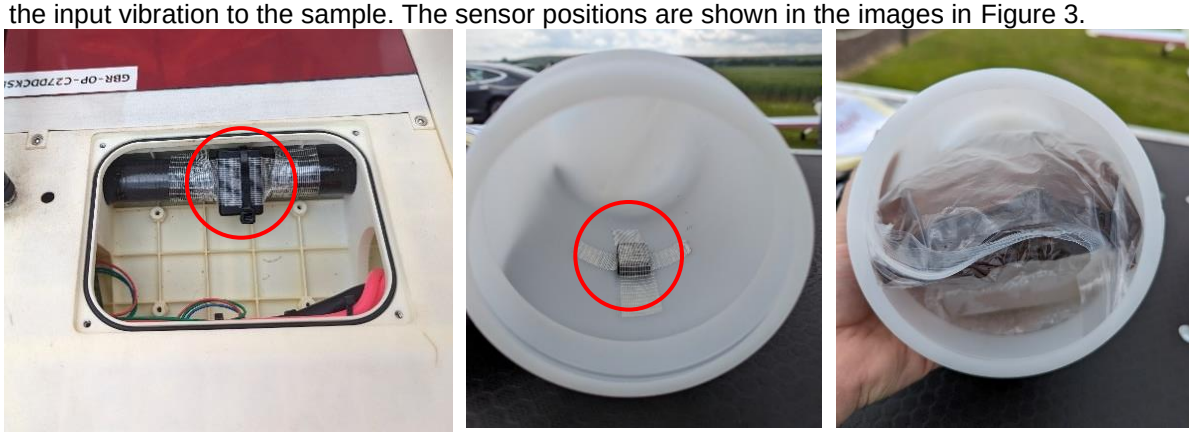
Figure 2: (a) Soton UAV Spotter drone used for this trial. Figure 2 (b) Flight path for flight testing at Draycot Airfield. Flight was 43mins in length covering approximatley 17km. Base map and data from OpenStreetMap and OpenStreetMap Foundation

3.2 Packaging and Payload

The payload is carried on Spotter by means of an underslung tube carrier as seen in Figure 2(a). The tube is a standard medical carrier known as a biobottle which is rigid high-density polyethylene bottle typically used to carry patient samples. For this example flight the payload consisted of three 100ml intravenous (IV) bags of the monoclonal antibody (mAb), Nivolumab. The packed biobottle can also be seen in Figure 3(c).

3.3 Instrumentation

Vibration levels during the example flight were recorded using triaxial MEMS data logging accelerometers (Axivity AX6, axivity.com) at a sampling rate of 1.6 kHz and a maximum range of ±16 g. Sensors were mounted directly on the airframe and within the payload to provide a reference for the input vibration to the sample. The sensor positions are shown in the images in Figure 3.



(a) (b) (c)

Figure 3 (a) Airframe sensor position. (b) Payload sensor poistion. (c) Loaded biobottle

4 VIBRATION ANALYSIS

Preliminary analysis of the recordings from both the triaxial accelerometers was undertaken to determine the appropriate recording to use, the correct equipment and any processing of the data that would be required. Overall vibration levels given in the following results are the root mean square (RMS) values, calculated as the standard deviation of the magnitude of the resultant acceleration vector (i.e. $r = \sqrt{(\sigma_x{}^2 + \sigma_y{}^2 + \sigma_z{}^2)}$). Octave band spectra were synthesised by first calculating the narrowband spectra and summing these values over the octave band.

Figure 4 shows power spectral densities (PSDs) of the resultant airframe acceleration and payload acceleration during the example flight. It can be seen from the PSDs that below approximately 40 Hz, vibration is negligible. The fundamental blade passing frequency of 58 Hz, and strong subsequent harmonics at approximately 115 Hz and 175 Hz, correspond to a rotor speed of about 7000 rpm. The figure also shows the amplification of acceleration from the airframe to the biobottle, possibly due to its mounting to the airframe.

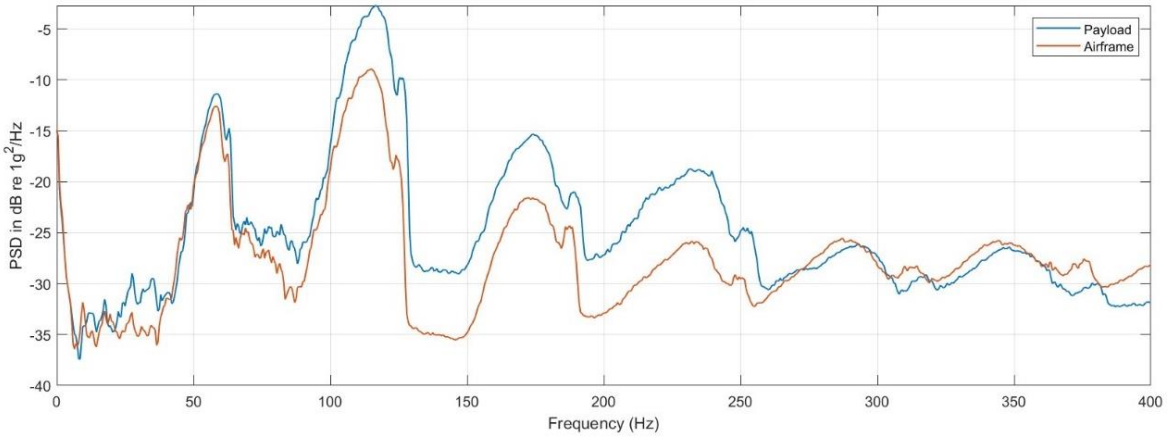


Figure 4: Power spectral densities of the resultant acceleration for the airframe sensor position and the payload.

5 FLIGHT REPLICATION

Flight replication was achieved through a standard vibration testing laboratory set up consisting of a laptop and signal controller to replicate the time history recording, an amplifier, shaker and accelerometer to complete the control loop and ensure a faithful replication.

The signal selected for replication was the biobottle recording as this represented the worst-case input due to the vibration levels being higher than the airframe recording. This represents the most conservative assumption in the case of the sensitive cargos. The vertical acceleration recorded on the spotter drone for the full duration of the 43 minute flight was replayed with a single 100ml IV bag sample affixed to the shaker table.

5.1 Laboratory Equipment

The shaker selected for use in this experiment is the Modal Shop 2110e Shaker which was capable of providing the frequency range required and identified in section 4. Whilst its peak to peak stroke length of 25mm may not be capable of replicating some lower frequency vibration, contributions below 40 Hz are negligible as noted in section 4, so should not have a significant impact on the accuracy of the replication. A high pass filter was applied to the flight data with a corner frequency of 25 Hz. The signal controller selected for the experimental set up was the Data Physics Abacus 901 (dataphysics.com). Recordings from the live flight trial, detailed in section 3, were uploaded and processed in the DP 900 software.

A flat shaker table to accommodate the medical samples was designed and manufactured and its natural frequency was engineered to be significantly above the frequency range of interest. The table was 200mm x 200mm x 8mm with a fundamental frequency of 628 Hz. Samples were then attached to the shaker table using adhesive tape .

Additionally, during the replication, a MEMS data logging accelerometers as described in section 3.3 as also affixed to the shaker table to record the actual vibration signal from the replication.

6 COMPARISON / RESULTS

Figure 5 shows the comparison of the PSD for the vertical direction and the resultant. Visually it can be seen that the vertical direction is closely replicated with the exception of below 25 Hz which was filtered out due to the stroke limitation as described in section 5.1. Above 25 Hz the replication is close with some deviation such as a 6 dB difference at 193 Hz and approximately 3 dB difference above 275 Hz.

In the resultant PSD there is up to a 9 dB difference primarily due to the missing lateral directions.

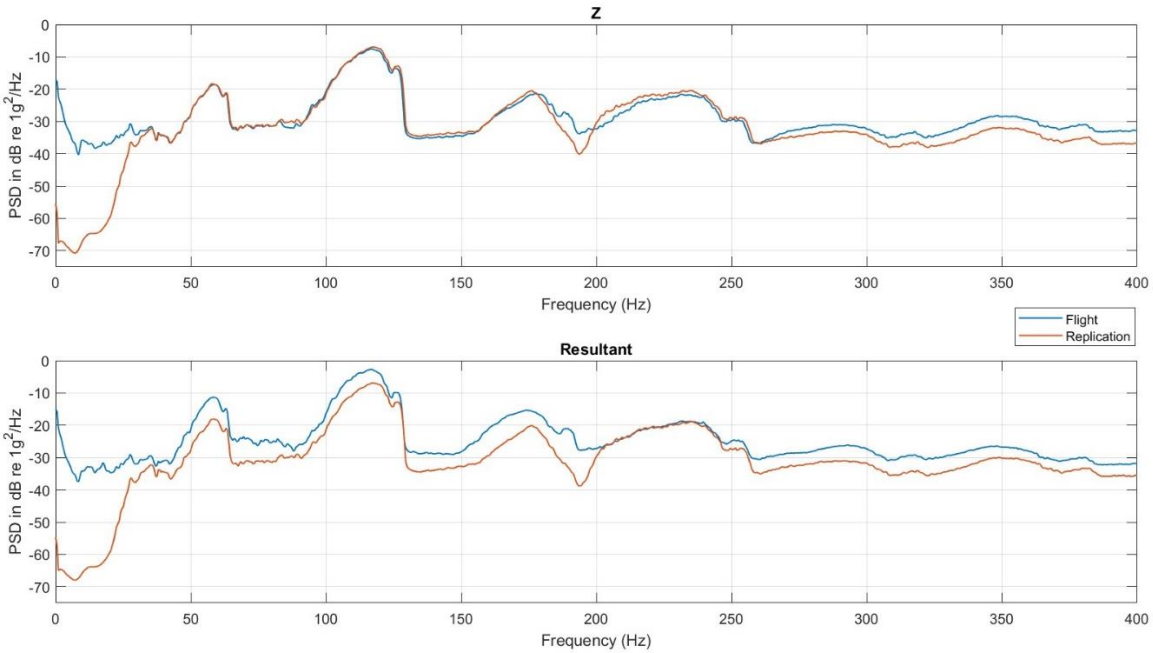


Figure 5: Power spectral densities for the Z direction and the resultant for the flight recording and the recording of the vibration replication.

7 CONCLUSIONS

In this case study and initial trial of vibration replication of drone flight has been undertaken and has demonstrated the practical feasibility of laboratory testing of products that require testing for drone flight. Additionally it has also identified limitations and next steps for developing testing protocols for this application. While the testing method was successfully completed there is notable difference between the flight recordings and the replication. It is not possible to conclusively state the significance of the difference between the recorded flight vibration and replicated vibration in the context of determining the suitability of cargos for a delivery method as the quality failure of different cargos may be sensitive to different parameters. Where vibration replication of flights is being used to demonstrate suitability of drones to deliver sensitive cargos in lieu of more comprehensive exploratory tests then accuracy in all key parameters is paramount. While if there is some understanding of the importance of key parameters then this may be an acceptable level of accuracy. The benefit of this flight replication testing is that these trials can be repeated and adapted to build on this work and progress the understanding without the need to repeat the live flight trials which both reduces cost, time and complexity of testing. There is a significant amount of work that can be built from this test which is discussed in the following final section.

8 FURTHER WORK

This paper presents only a first trial of vibration replication of a drone flight and further work is required to refine this protocol and ensure its robustness as a method for determining the safety of medical products for patient use. This trial should be repeated with different flight recordings and samples to better understand the origins of the errors particularly in the time domain.

A second measure of the effectiveness of this method of replication, and ultimately as a method of testing the stability of liquid medicine for delivery by drone, is to ensure that the change of quality of medicine is the same when flown in an actual drone and when tested using a replicated vibration profile. As discussed in Section 1.1 the testing of the quality of the medicines for patient use is closely defined by the MHRA. Samples of Nivolumab that were carried in the live flight trial along with sampled exposed to the replicated vibration will undergo comprehensive quality testing in line with this guidance, the results of these tests will be subject of a future publication.

Testing should also be undertaken to investigate the effects on accuracy and pharmaceutical quality when single orthogonal directions are replicated versus the replication of all three orthogonal directions. Additional trials could be undertaken to investigate the potential for utilising time compression to reduce overall testing time.

Further series of controlled trials should be undertaken to develop a systematic test to determine products' sensitivity to different vibration parameters such as frequency, magnitude and duration. Finally, as further recordings of real drone flights are collected and analysed standard/ generalised PSD profiles could be developed to align with existing road-based testing protocols as discussed in section 1.2.

9 REFERENCES

1. De Silvestri, S., et al., *Challenges for the Routine Application of Drones in Healthcare: A Scoping Review.* Drones, 2023. **7**(12): p. 685.
2. Zipline. *Zipline Homepage*. 2024 [cited 2024 07/08]; Available from: https://www.flyzipline.com/.
3. Rogers, K. *Drone startup Zipline hits 1 million deliveries, looks to restaurants as it continues to grow*. 2024 [cited 2024 08/07]; Available from: https://www.cnbc.com/2024/04/19/autonomous-drone-startup-zipline-hits-1-million-deliveries.html#:~:text=Drone%20startup%20Zipline%20hits%201%20million%20deliveries%2C%20looks%20to,as%20it%20continues%20to%20grow&text=Autonomous%20delivery%20drone%20startup%20Zipline,autonomous%20miles%20across%20four%20continents.
4. O'Connell, B. *NHS to scale up drone delivery programme of critical medical supplies using Apian and Zipline*. 2023 [cited 2024 07/08]; Available from: https://www.northumbria.nhs.uk/media-centre/news-and-blogs/news-stories/nhs-scale-drone-delivery-programme-critical-medical-supplies-using-apian-and-zipline#6ee0174a.
5. Oakey, A., Cherrett, T, *A drone service to support the Isle of Wight NHS in the UK*, in *ITS*. 2022, Proceedings of the 14th ITS European Congress, Toulouse, France 30 May-1 June 2022.
6. Oakey, A., Waters, T., Zhu, W. Q., Royall, P. G., Cherrett, T., Courtney, P., Majoe, D. and Jelev, N., *Quantifying the Effects of Vibration on Medicines in Transit Caused by Fixed-Wing and Multi-Copter Drones.* Drones, 2021. **5**(1).
7. Skyports. *NHS launches UK's first COVID test drone delivery service in Scotland*. 2021 [cited 2023 17/07/23]; Available from: https://skyportsdroneservices.com/nhs-launches-uks-first-covid-test-drone-delivery-service-in-scotland/.
8. Zhu, W., Oakey, A., Royall, P. G., Waters, T. P., Cherrett, T., Theobald, K., Bester, A. and Lucas, R., *Investigating the influence of drone flight on the stability of cancer medicines.* PLOS ONE, 2023. **18**(1): p. e0278873.
9. Theobald, K., et al., *Stability of Medicines Transported by Cargo Drones: Investigating the Effects of Vibration from Multi-Stage Flight.* Drones, 2023. **7**(11): p. 658.

10. Hii, M.S.Y., Courtney, P. and Royall, P. G., *An Evaluation of the Delivery of Medicines Using Drones.* Drones, 2019. **3**(3).
11. (ICAO, I.C.A.O., *Annex 18 to the Convention on International Civil Aviation—The Safe Transport of Dangerous Goods by Air, 4th Edition*. 2011, International Civil Aviation Organization:: Montreal, QC, Canada.
12. (ICAO), I.C.A.O., *Technical Instructions for the Safe Transport ofDangerous Goods by Air (Doc 9284), 2019–2020 Edition*. 2018, International Civil Aviation Organization: Montreal, QC, Canada, 2018.
13. Vehicle Certification Agency, *Crash protected containers for dangerous goods carried by remotely piloted aircraft system*. 2022, VCA Dangerous Goods Office: Wesley House, Bull Hill, Leatherhead, Surrey, KT22 7AH, United Kingdom.
14. (CAA), C.A.A., *CAP2555: Guidance on the Carriage of Dangerous Goods as Cargo for UAS/RPAS Operators in the Specific Category*. 2023: Civil Aviation Authority,Aviation House, Beehive Ring Road, Crawley,West Sussex, RH6 0YR.
15. Agency, M.a.H.p.R., *European Commission Guidelines of 7 March 2013 on Good Distribution Practice of medicinal products for human use*. 2013: Official Journal of the European Union: C343/1.
16. Agency, M.a.H.p.R., *Rules and Guidance for Pharmaceutical Distributors 2017 (The Green Guide).* 2017.
17. International Organization for Standardization, *ISO 13355:2016 Packaging — Complete, filled transport packages and unit loads — Vertical random vibration test*. 2016. p. 9.
18. American Society for Testing and Materials, *ASTM D4169-22 Standard Practice for Performance Testing of Shipping Containers and Systems*. 2022. p. 17.
19. American Society for Testing and Materials, *ASTM D4728-17 Standard Test Method for Random Vibration Testing of Shipping Containers*. 2022. p. 6.
20. National Standard of the People's Replublic of China, *GB/T 4857.23 Packaging -- Basic tests for transport packages -- Part 23: Random vibration test method*. 2021.
21. Zheng, D., Chen, J., Lin, M., Wang, D., Lin, Q., Cao, J., Yang, X., Duan, Y., Ye, X., Sun, C., Wu, D., Wang, J. and Chen, K., *Packaging Design to Protect Hongmeiren Orange Fruit from Mechanical Damage during Simulated and Road Transportation.* Horticulturae, 2022. **8**(3): p. 258.
22. Johannessen, K.A., Wear, N. K. S., Toska, K., Hansbo, M., Berg, J. P. and Fosse, E., *Pathologic Blood Samples Tolerate Exposure to Vibration and High Turbulence in Simulated Drone Flights, but Plasma Samples Should be Centrifuged After Flight.* IEEE journal of translational engineering in health and medicine, 2021. **9**: p. 4000110.