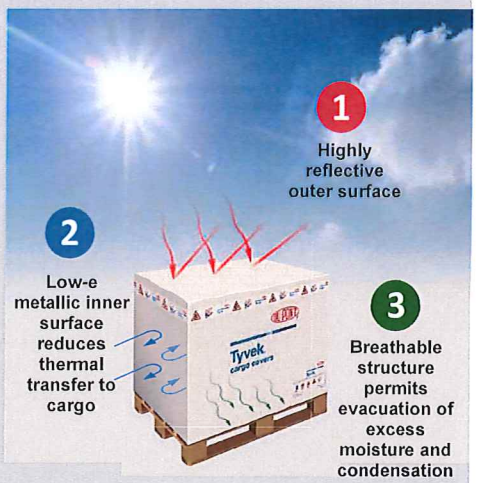
Tyvek® Xtreme™ W50

Performance Qualification Report

TYVEK® XTREME™ W50 CARGO COVERS

TRIPLE PROTECTION



Tyvek® Xtreme™ W50 Cargo Covers employ a unique <Triple Action> to address the heat flow mechanisms that govern the temperature swings and movements typically found in cargo distribution.

Tyvek® Xtreme™ W50 from DuPont is a new generation of lightweight, low-bulk and breathable cargo covers combining state-of-the-art radiation protection with thermal insulation to provide an optimal series of properties for the protection of pharmaceuticals and perishables in transit.

Designed to 'bridge the gap' between single-skin thermal covers and bulky quilted thermal blankets, the new cover combines double-sided reflectivity with a high efficiency thermal layer giving both a radiant shield and a conduction barrier. It has also been engineered to be vapour permeable yet fully weather-resistant, allowing protected pallets to evacuate condensation by 'breathing' whilst providing dependable protection from rain, snow and wind. The result is a cost-effective, fully contoured, off-the-shelf protective envelope for the protection sensitive merchandise against high and low temperatures during transit.

Triple Protection

Tyvek® Cargo Covers typically exhibit a three-stage protection which differentiates Tyvek® from other cargo covers on the market. The new generation Tyvek® Xtreme™ W50 adds a high efficiency insulant to the cover structure which extends its performance particularly at low temperatures.

The inner and outer reflective performance of Tyvek® combined with the new product's mass thermal barrier creates a protective envelope suitable for resisting the ambient and direct temperature variations found in long-haul situations such as intercontinental CRT freight lanes. The product is especially useful for cases where there are transient exposures to very low ambient temperatures and for routes where there is a potential for sizeable temperature swings.

Tests in the field have shown that low-emissivity Tyvek® offers significantly better thermal protection under real-life conditions than many of the other cover materials and systems that are in widespread use for passive CRT protection. In fact, research by DuPont has confirmed the findings from independent studies which show that some commonly used cover materials actually exacerbate the 'greenhouse effects' of solar exposure, even in sunny-cold environments. So although these covers may provide some protection against ambient temperature deviations they fall down in real life situations due to their ineffectiveness against solar gain incidents - the prime cause of significant temperature excursions.

And, with their breathable layer of fibrous insulant, Tyvek® Xtreme™ W50 covers also provide several hours of extended cold chain protection. This makes them ideal for protecting 'controlled room temperature' products. They can also be used in combination with other insulating products to supplement protection for 2°C - 8°C protection.

ABOUT PRODUCT QUALIFICATION

It is the responsibility of shippers and their supply chain partners to conduct validation exercises on individual transit lanes to demonstrate that all the elements and parties involved in the entirety of the distribution process, from factory to consumer, work together to provide an outcome which is safe, secure and fit for purpose.

Transport validation covers the entire distribution process including all third parties. It is a process that must embrace the entire mix of methods and SOPS relating to personnel, equipment, packaging, transport, storage, measurement, monitoring and recording. For this to happen shippers must rely on products and materials that have been 'qualified'. For further information on the qualification process please refer to Appendices A & B.

OBJECTIVE OF PROGRAMME

The purpose of the Tyvek® Xtreme™ W50 qualification programme was to use thermal mapping data to provide documented evidence that a cargo pallet protected with a Tyvek® Xtreme™ W50 cover gains robust protection against exterior environmental conditions including exposure to both high and low ambient temperatures and the effects of direct solar radiation.

TEST METHODOLOGY

The methodology involved assessing the impact of different temperature exposures to measure protective performance and assess the level of associated risk. The results were correlated against a selection of alternative materials that are commonly used for the passive protection of pharma merchandise.

SCOPE

The Qualification exercise has two elements:

- Static (Operational) Qualification including chamber tests and external exposure tests.
- Dynamic Route (Performance) Qualification

The static tests were designed to identify the operating envelope within which the Tyvek® Xtreme™ W50 cover will function effectively. The static tests included chamber tests and outdoor exposure tests. The dynamic tests on the other hand were conducted as part of a genuine shipping exercise designed to demonstrate that the Tyvek® Xtreme™ W50 product functions as intended under real-life conditions as part of an overall cool-chain system. Note that the dynamic exercises were not designed to attest the product's operating parameters.

(For further information on the relationship between these two qualification components see Appendix B)

PRODUCT SPECIFICATION

The new Tyvek® Xtreme™ W50 Cargo Cover comprises a strong, continuous-filament, fibrous insulation layer laminated to a tough overlay of non-woven Tyvek® material. By combining a low-emissivity aluminium layer with both a highly reflective outer surface and a high efficiency inner insulation layer, the new cover performs both as a radiant shield and a conduction barrier.

The special insulative fleece used in Tyvek® Xtreme™ W50 is durable and better able to maintain its thermal properties and withstand physical manhandling than plastic film and bubble-based alternatives.

Research by DuPont and others has clearly demonstrated that the real enemy when it comes to unwanted temperature excursions in air cargo scenarios is not necessarily ambient temperature differences but, in many cases, the 'greenhouse effects' of exposures, even brief ones, to solar radiation. This means that a material's thermal reflectivity and the solar exposure risks must be considered in addition to the insulation characteristics, when specifying CRT pallet covers.

MATERIAL SPECIFICATION

Fig 1

PROPERTY	VALUE	TEST METHOD
Basis weight(1)	330 g/m² ± 15 g/m²	DIN EN ISO 536 (96)
Tensile Strength*(2)	MD 155 ± 25 N/5cm	EN 12311-1 (99)
	XD 130 ± 20N/5cm	
Tensile Elongation*(2)	MD 9% ± 3%	EN 12311-1 (99)
	XD 14% ± 5.5%	
Tear Resistance (nail shank) *(2)	MD 60 ± 20 N	EN 12310-1 (99)
	XD 55 ± 15 N	
Emissivity*	16 % ± 6 %	ASTM C1371
Light Reflection (400-700 nm)*	91.3% ± 3%	ASTM E1164
Moisture Vapor Transmission*(3)	1300 ± 600 g/m² / 24h	DIN EN ISO 12572 C
Water Pressure (Hydrostatic Head)*(4)	>140 cm H_2O	DIN EN 20811 (92)
Resistance to Penetration of Water *(2)	W1 PASS	DIN EN 1928-A (00)
Thermal Conductivity (at 0°C)**	0.0288 W/mK	ASTM C518
Thermal Resistance (at 0°C)*	0.3035 m²K/W	
	1.72 ft² °F. hr /BTU	ASTM C518
	4.37 ft² °F. hr /BTU	

MD/XD: Machine direction/Cross machine direction
* Reflective layer property
** Insulating layer property
(1) Sample size 100cm²
(2) Modified for sample preparation before testing as per EN 13859-1 (2010) & EN 13859-2 (2010)
(3) Results based on multi-layer testing; 100% RH in the cup; 2.5 m/s air velocity above the cup; 30 min time interval
(4) Rate of use 60 cmH_2O/min

TEST REGIME PROFILE

Fig 2

1	HYDERABAD	External Temperature Test (Hot) Duration: 24 hrs Weather: Cloudy Temp: +17.5°C to +37°C	
2	HYDERABAD	Pre-conditioning Duration: 48 hrs	
3	HYDERABAD	Tarmac Transfer Duration: 3 hours (predetermined) Weather: Part cloudy Temp: +24°C to +44°C	
4	HYDERABAD - DUBAI	Flight Leg 1: Hyderabad - Dubai Duration: 3 hours 45 minutes	
5	DUBAI	Tarmac Transfer inbound Duration: 6 hours (predetermined) Weather: Partly cloudy + rainshowers + thunderstorm Temp: +19°C to +24°C	
6	DUBAI - OSLO	Tarmac Transfer outbound Duration 1.5 hours Weather: Partly cloudy Flight Leg 2: Dubai - Oslo Duration: 7 hours 15 minutes	
7	OSLO	Tarmac: Oslo Duration: 9 hours (predetermined) Weather: Cloudy/clear Temp: -6°C to -9°C	
8	OSLO - LUXEMBOURG	Road Journey (non-temperature controlled) Duration: 70 hours Distance: 1300 km	
9	LUXEMBOURG	External Exposure Tests Duration: 72 hours Weather: Clear Temp: -3°C to +10°C	

THERMAL CHAMBER TESTS

Euro Pallets 48" (1 x 0.8 x 1.2 m)

32 boxes

4 rows - 8 boxes per row

100 ± 10 Kg for liquid thermal mass

Duration = 1 or more cycles

Conditioning: 20°C ± 2°C

Thermal chamber from -20°C to +40°C

Position of probes: inside all the corner boxes and center of the pallet, taped to the thermal mass

Measurements taken inside and outside the boxes

DATA LOGGING DEVICES

Measurement range: -30°C to +60°C

Complies to CE guidelines 2004/108 EG

Resolution: 0.1°C

Accuracy: +/- 0.5°C

Data memory: 40.000 readings

Sample rate: 1 min - 24h

Battery runtime: up to 2 years

STATIC (OPERATIONAL) TESTS

Tyvek® Operational Qualification

Thermal chamber testing of Tyvek® covers is a vital element of the overall qualification process and the first stage of tests involved a series of operational qualification (OQ) studies. These studies concerned chamber-testing to subject the covers to simulated environmental conditions of a sufficiently extreme nature to demonstrate performance under relatively severe conditions.

These simulation exercises were then replicated to demonstrate repeatability and consistency. The results established the performance margins of the Tyvek® product and provided benchmark data for validation under dynamic field conditions.

The first part of the temperature validation exercise involved conducting a series of static tests designed to measure the performance of the Tyvek® Xtreme™ W50 covers in simulated summer and winter conditions. The effects of prolonged exposure to the sun were also measured along with the ability of the covers to protect against cold.

Fig 3

STATIC CHAMBER TEST 40°C AMBIENT: Average Sensor Temperatures

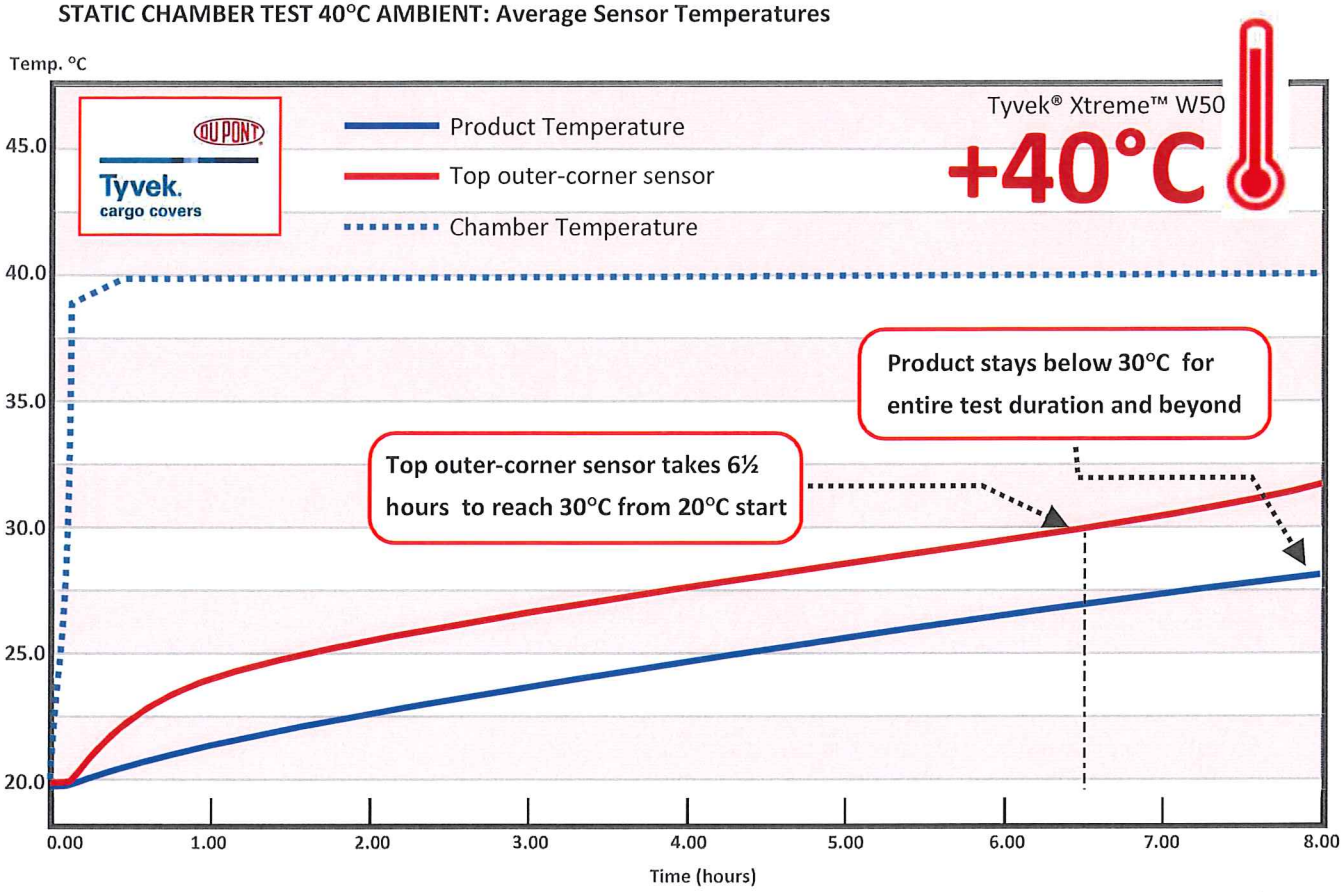
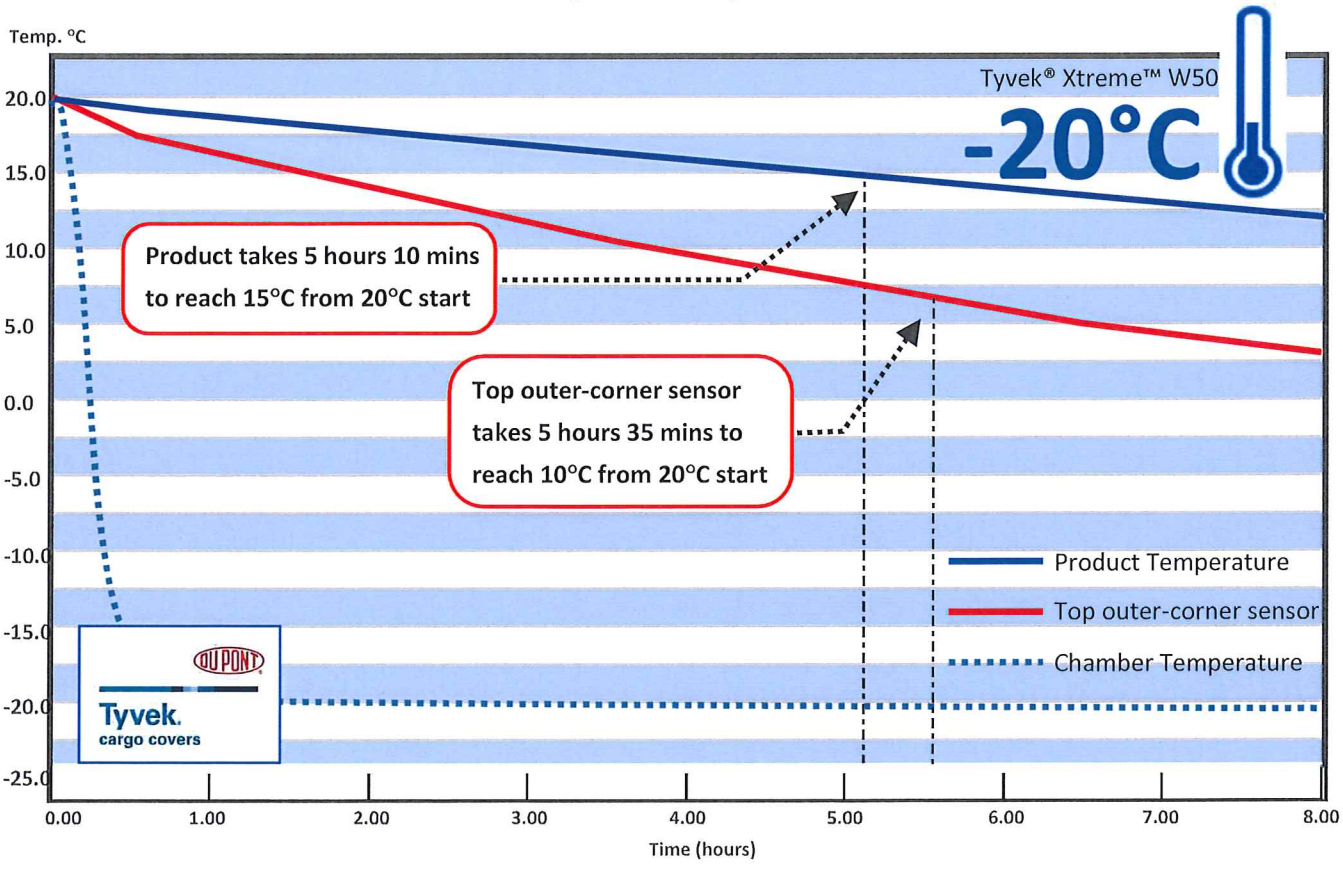


Fig 4

STATIC CHAMBER TEST -20°C AMBIENT: Average Sensor Temperatures



SOLAR RADIATION TESTS

Euro Pallets 48" (1 x 0.8 x 1.2 m)

32 boxes

4 rows - 8 boxes per row

Solar intensity > 1000 W/m²

100 ± 10 Kg for liquid thermal mass

Duration: 72 hours

Conditioning: 20°C ± 2°C

Temperature Loggers: 11 total

Position of the probes: Inside all the corner boxes, center of the pallet, taped to the thermal mass, plus one on top of the pallet on the outside to record outer surface temperature.

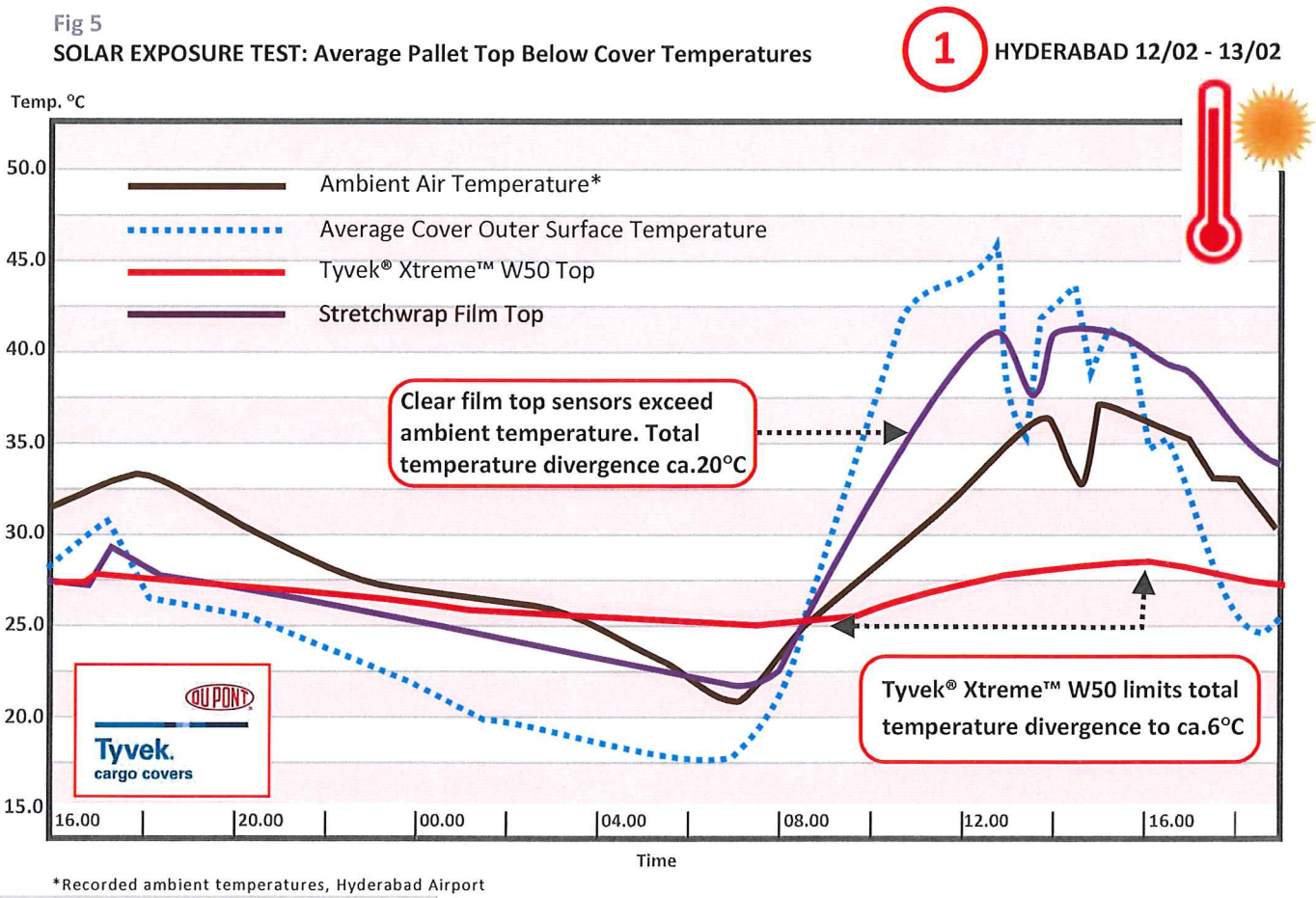
OUTDOOR SOLAR RADIATION TESTS

The Tyvek® qualification programme took particular recognition of the effects of solar radiation since this is widely recognised as the biggest weakness in the pharmaceutical coolchain. During the controlled tests on Tyvek® covers, and in virtually all independent trials, these damaging, but oft-ignored, solar effects were clearly evident.

According to IATA, more than 50% of temperature excursions occur during relatively 'uncontrolled' external handling operations such as loading, unloading, marshalling and apron transfer. It has been estimated by one authoritative source that up to 5% of all pharma transportation events involve a temperature deviation from plan with solar radiation and its associated 'greenhouse effects' being the principle cause of undesirable temperature spikes during transportation.

Fig 5

SOLAR EXPOSURE TEST: Average Pallet Top Below Cover Temperatures



*Recorded ambient temperatures, Hyderabad Airport

The test shipment on PMC pallet at unloading in Oslo

PURPOSE OF THE DYNAMIC ROUTE PERFORMANCE QUALIFICATION

The aim of the Tyvek® Dynamic Route PQ is to demonstrate that the static Operational Qualification results are applicable to real-life conditions and that the measured performance patterns are mirrored in the field.

DYNAMIC/ROUTE (PERFORMANCE) QUALIFICATION

Objective

The purpose of the temperature performance validation was to provide documented evidence that a cargo pallet covered with the DuPont Tyvek® Xtreme™ W50 Cargo Cover provides continuous and reliable protection against temperature and weather related impacts during transportation and storage in both hot (sun exposure, tarmac conditions, heat radiation, etc.) and cold (temperatures below freezing, windchill, etc) ambient conditions.

A two-leg "general freight' air journey followed by a 1300km road leg was devised in order to appraise the hot and cold performance of the Tyvek® Xtreme™ W50 cover in real-life conditions. Prior to the air legs a 24 hour solar test was conducted in Hyderabad. At the end of the road trip the pallets were monitored for a further 72 hours in external ambient conditions in Luxembourg.

A standard Euro pallet covered with a Tyvek® Xtreme™ W50 cover was prepared as a specimen shipping sample for live assessment. An identical pallet load covered with clear stretch-wrap film was also assembled for comparative purposes. Cartons on the pallets were secured with straps before adding the Tyvek® Xtreme™ W50 cover or the stretch-wrap. This was to make sure the load was fully stable during the entire transportation and warehousing exercise.

Fig 6 **THREE-LEG HOT/COLD QUALIFICATION ROUTE**

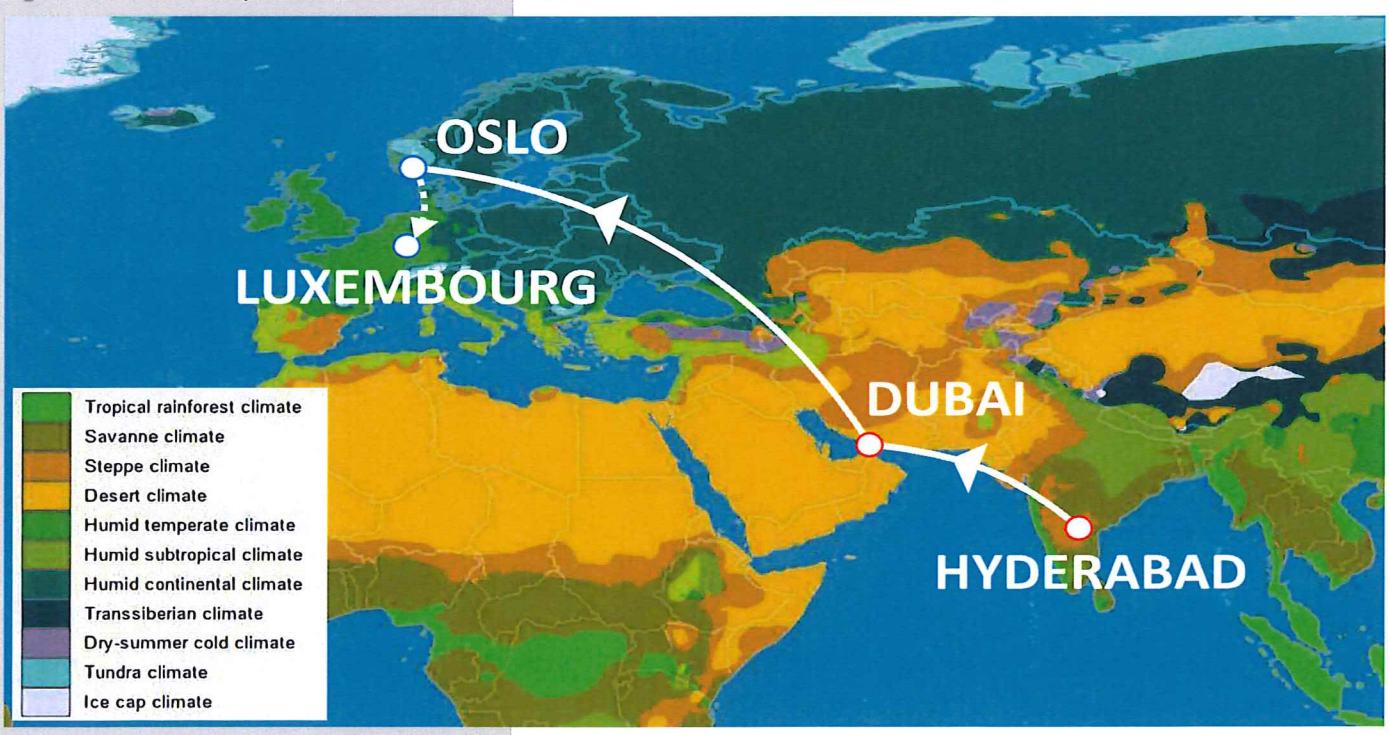
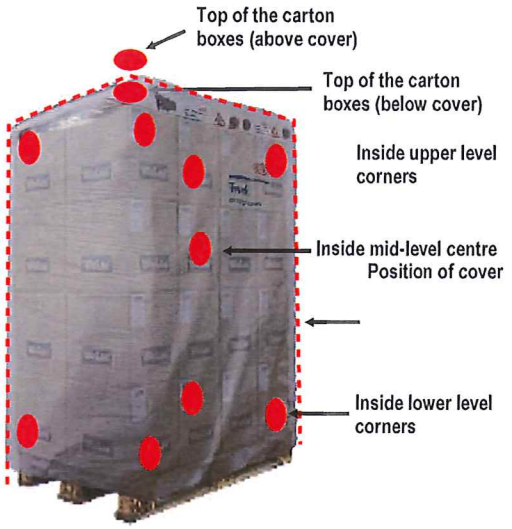


Fig 7

Positioning of temperature loggers



Euro Pallet 80 x 120 x 120cm high (incl. pallet 15cm)
32 carton boxes: 386 x 286 x 274mm (0.97m³)

DYNAMIC PERFORMANCE & EXTERNAL LOW TEMPERATURE TESTS

Euro Pallet 80 x 120cm, 135cm high (including pallet 15 cm)
32 box of 386 x 286 x 274 (0.97m³)
4 rows - 8 boxes per row
Boxes double wall corrugated cardboard
Each box containing 3 x 1L bottles
Total pallet weight including load, pallet and cover = c. 140 kg
Measurements inside and outside the boxes and outside of cover
Conditioning: 20°C ± 2°C
Duration = 72 hours
Position of the data-logger probes: 11 total: in boxes - each corner, center of pallet outside boxes, top below cover, top above cover
Data polling frequency: 300 secs

Nine data-loggers per pallet were placed inside carton boxes , a further data-logger was placed on top of the cargo under the cover and another was placed outside the cover to measure external temperature.

Fig 7 shows the designated pallet configuration and the location of the thermal sensors in the corners of the pallet, regarded as the most sensitive points for temperature excursions during shipment. The sensors used were calibrated to an accuracy of +/- 0.5°C.

The test was conducted with standard Euro pallets loaded with a total of 32 boxes in 4 layers. The boxes were made of double-walled corrugated board and each of these contained three 1.0 litre plastic bottles of water representing a typical medium-mass pharma product. The total net water volume of the pallet is 96 litres and this constitutes +/- 8.5% of the entire pallet volume. The load was restrained on the pallet with standard plastic strapping.

Since the air temperature under the cover and inside the boxes can fluctuate very rapidly, each data logger was placed so that its temperature sensor was in contact with one of the bottles of water in each box, and was then taped in place. This was to allow the sensors to record as closely as possible the product temperature, which was more relevant to the purpose of this test. Exceptions were the two data loggers placed on top of the top layer of boxes, one under the cover and the other on the outside of the cargo. These recorded the temperature of the outer surface of the centre top carton box and of the outer surface of the cover respectively.

Pallet 1: Tyvek® Xtreme™ W50, a high-performance cargo cover featuring a breathable silver-coated Tyvek® material laminated to an eco-friendly 250gsm polyester fleece.

Pallet 2: Stretch-wrap polyethylene film

Pre-conditioning

Pallets were assembled in Hyderabad (India) and preconditioned in a warehouse at +/- 20°C for 48 hours before being transported to the airport in a temperature-controlled truck. At time of pick-up the temperatures were checked and all found to be within an acceptable range.

Fig 8

CUSTOMS CLEARANCE + PMC BUILD: Pallet Top Temperature **2** **3** **HYDERABAD 15/02 - 16/02**

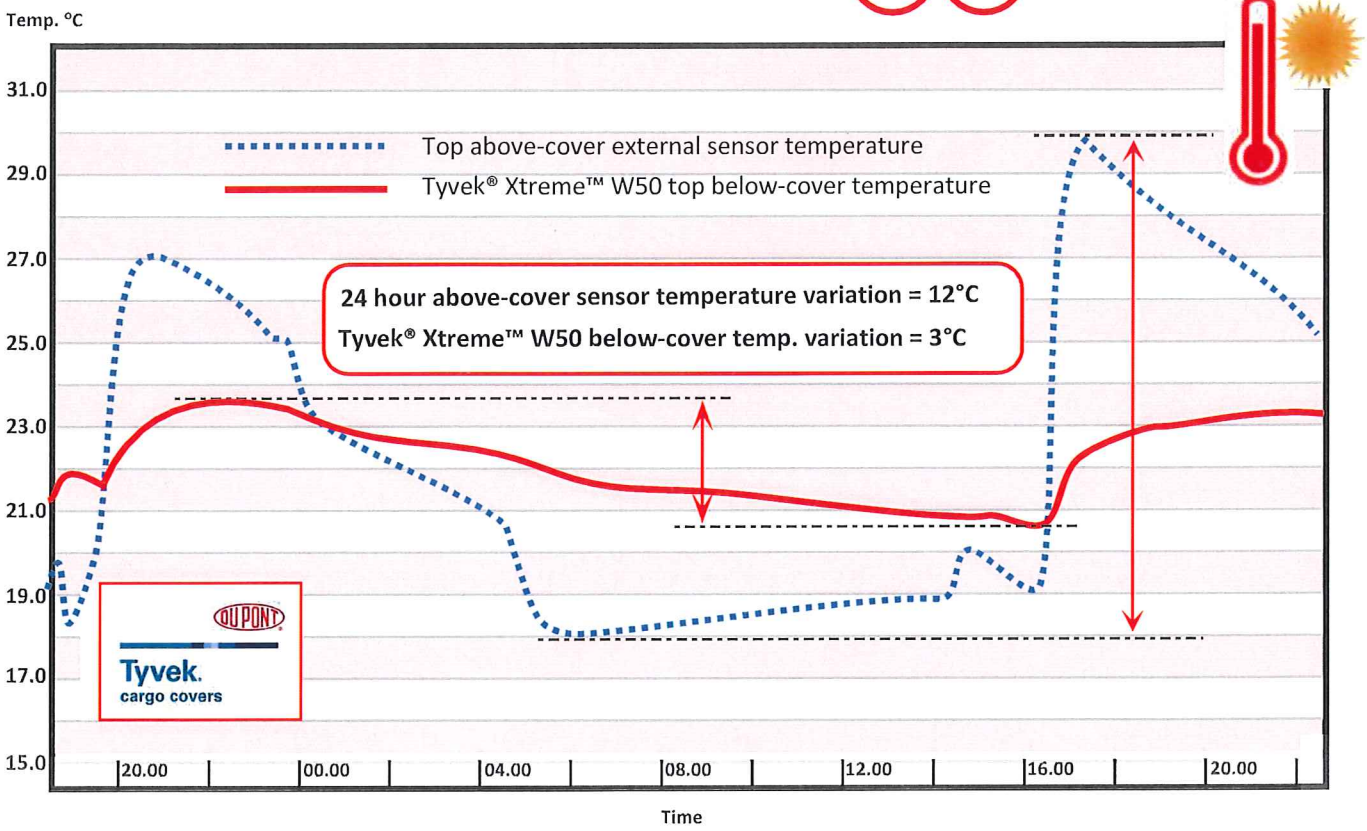


Fig 9

LOADING HYD/FLIGHT TO/UNLOADING DXB; STORAGE : Pallet Top Temp. **4** **5** **HYDERABAD - DUBAI 17/02 - 18/02**

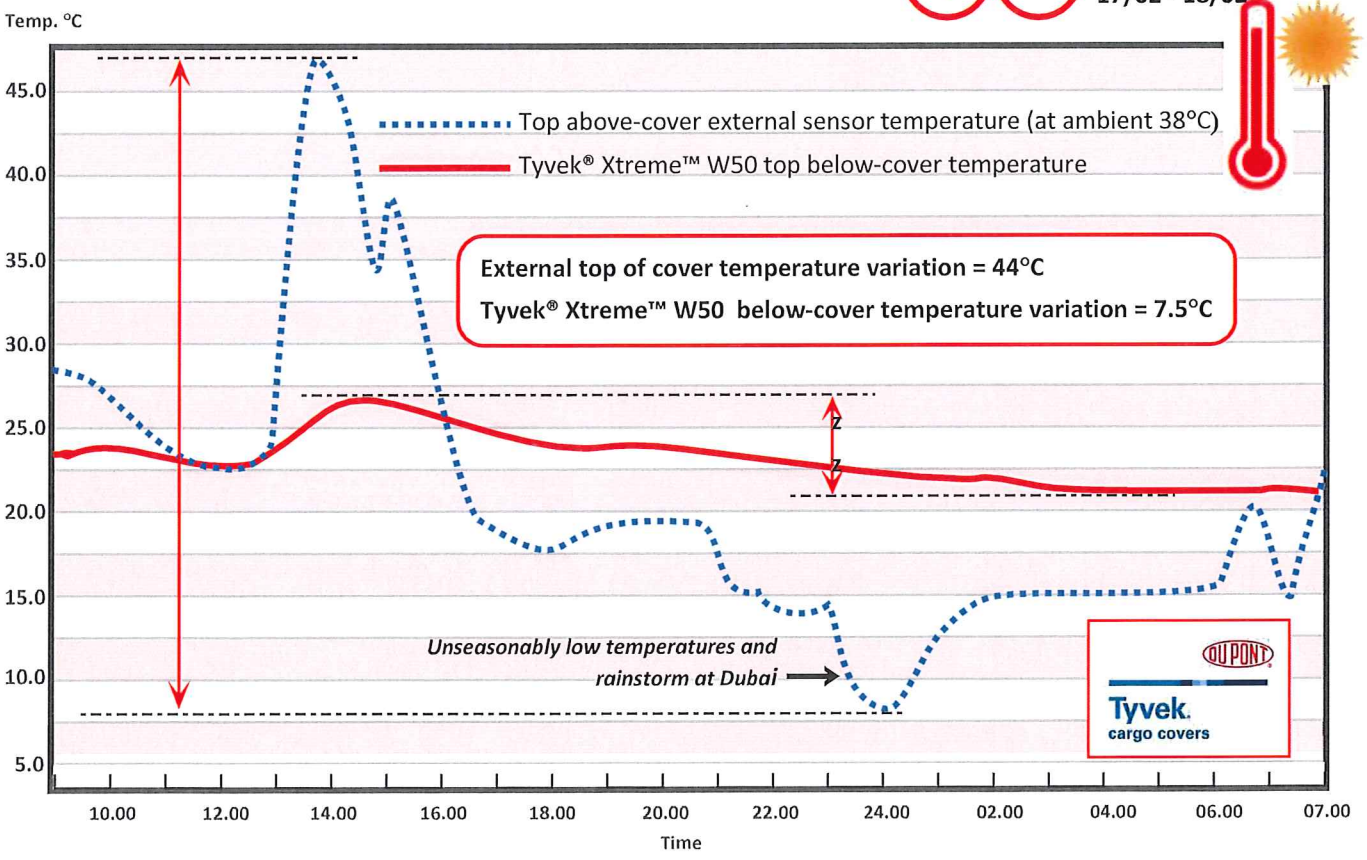
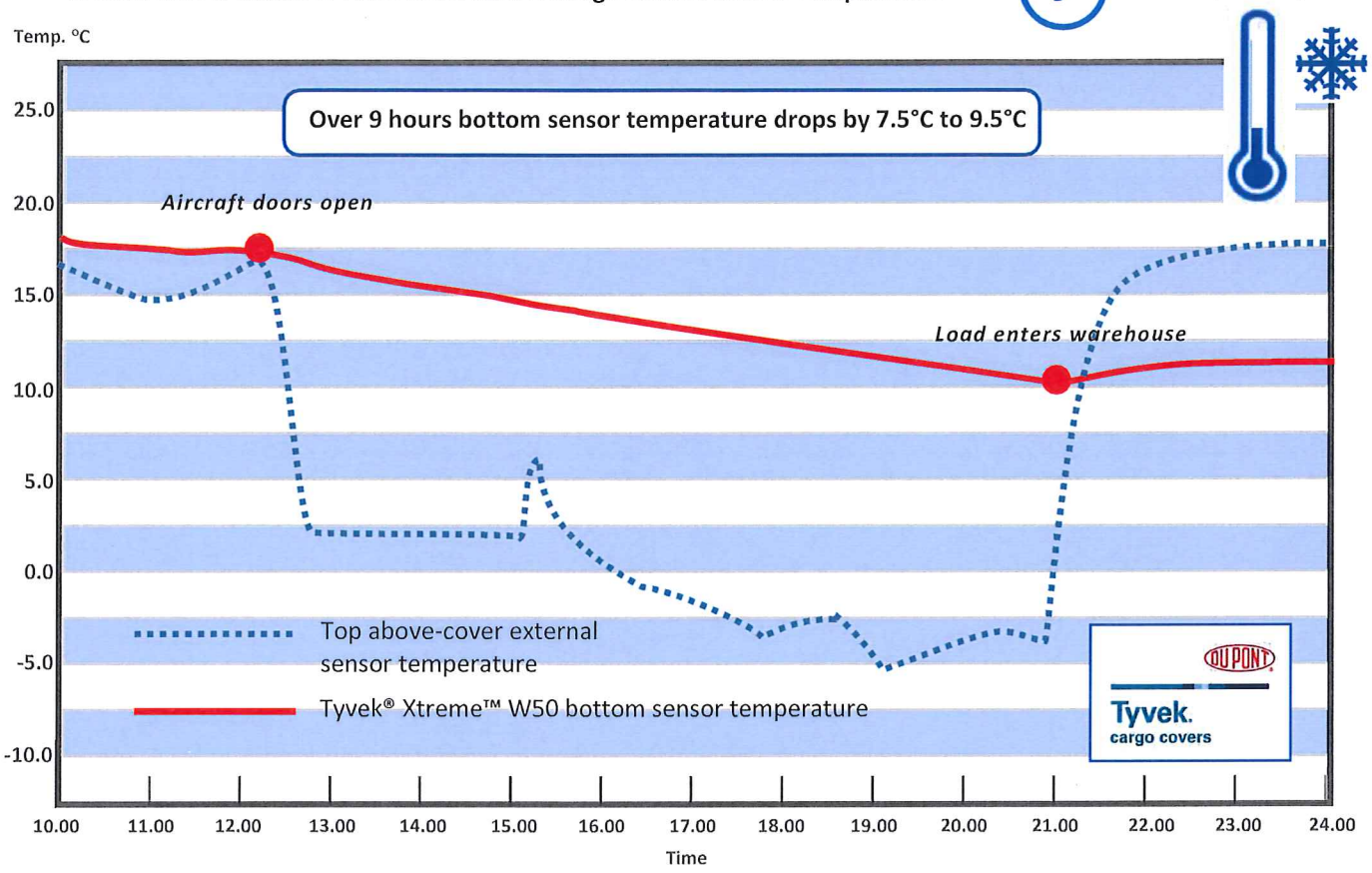


Fig 10

UNLOADING & TARMAC TIME OSL: Pallet Average Bottom Sensor Temperature

7 OSLO 18/02 - 19/02



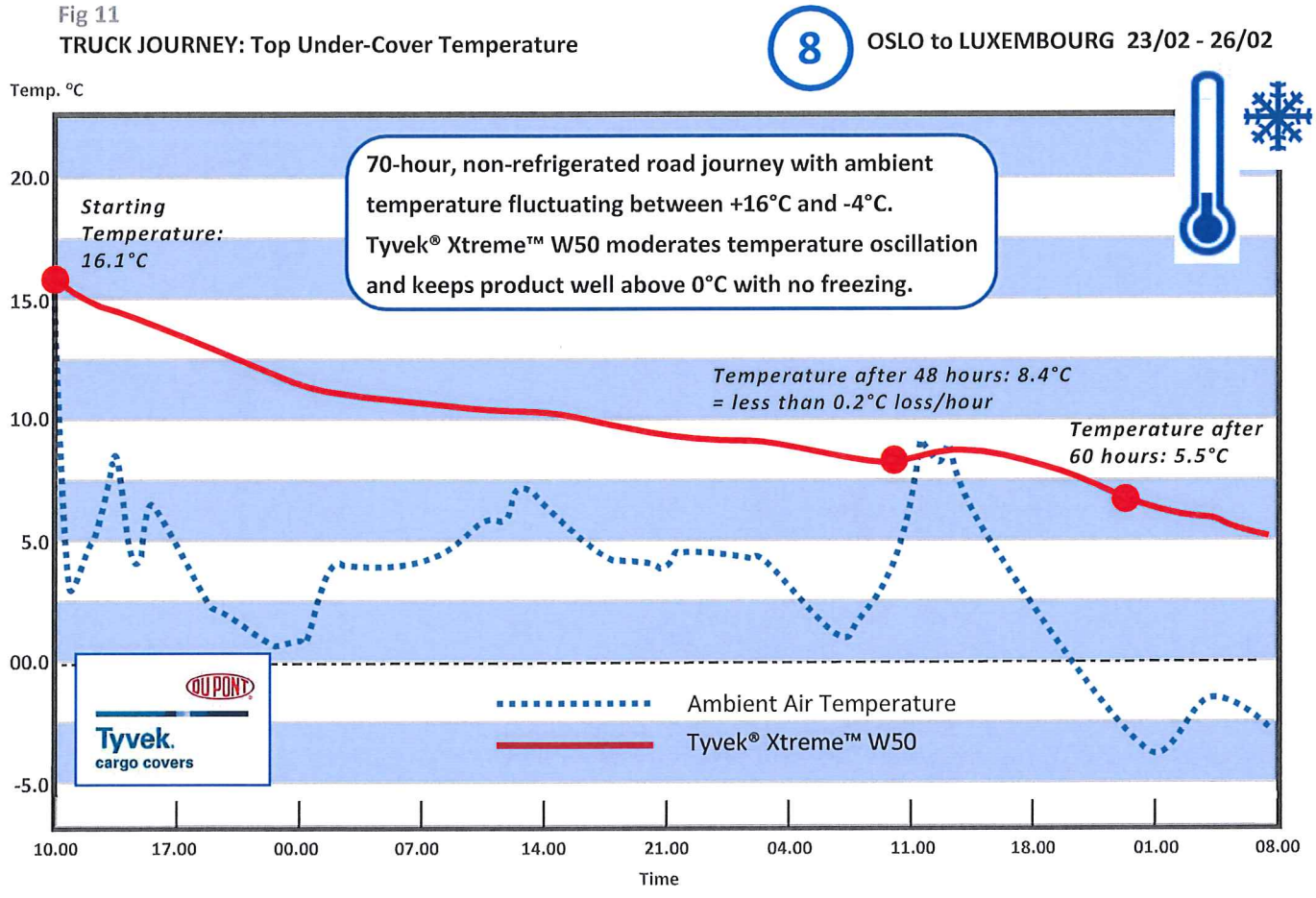
1300km road journey using non-temperature-controlled transport

ROAD TRANSPORT LEG

The third leg of the dynamic qualification involved a 1300km road trip by curtain-sided truck (non-temperature controlled) from Oslo to Luxembourg. This segment of the validation route was designed to observe and measure the performance of the Tyvek® Xtreme™ W50 under the handling and environmental conditions associated with long-haul road transport.

Fig 11

TRUCK JOURNEY: Top Under-Cover Temperature



Pallets on test during external exposure trial

OUTDOOR SOLAR RADIATION TESTS

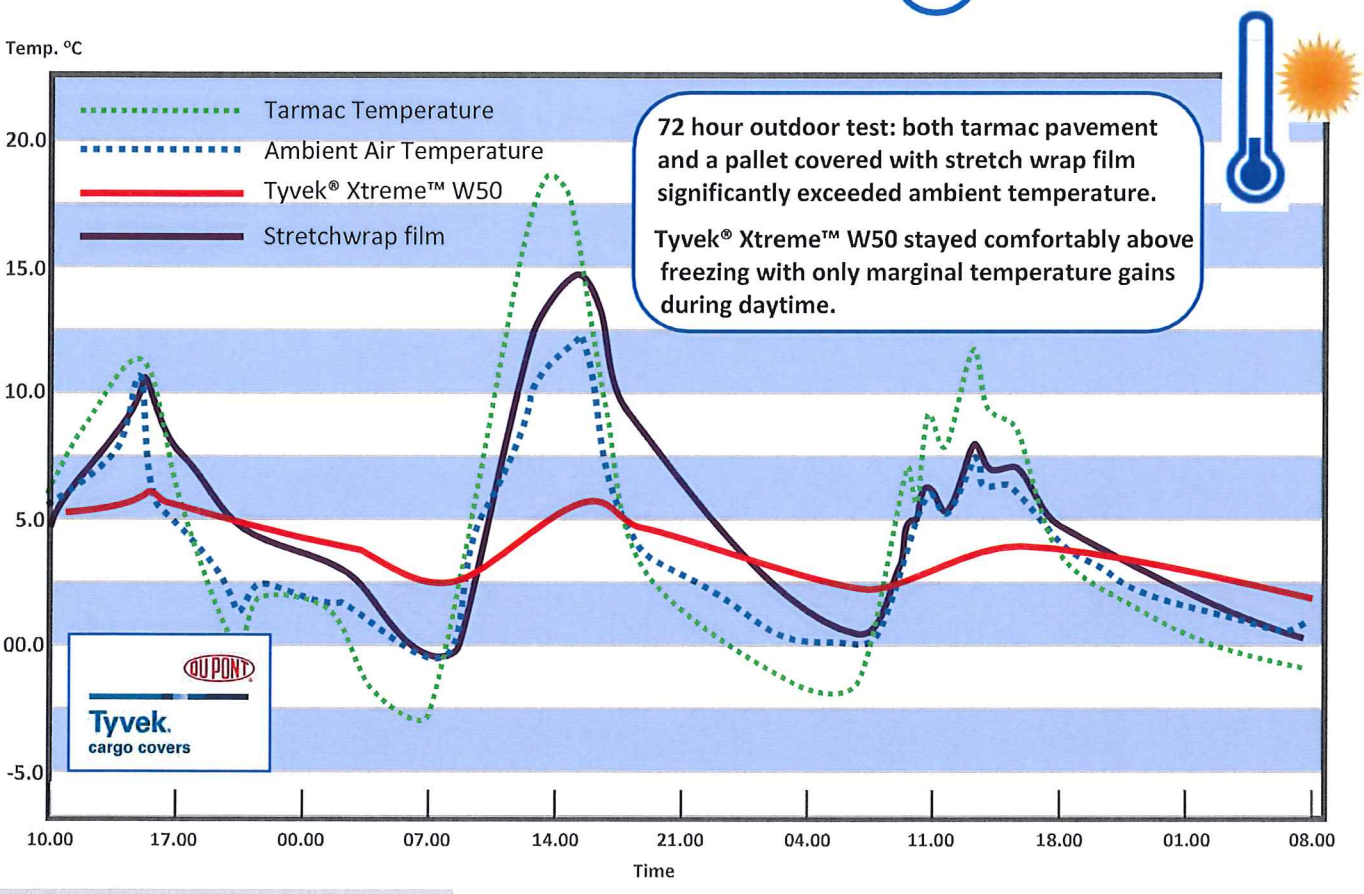
Exposure to solar radiation is known to be the most important cause of rapid temperature changes during outdoor cargo movements where ambient temperatures are high, especially in regions close to the equator. However, it is not always recognised that solar exposure can cause significant heating of cargos even at higher latitudes where ambient temperatures may not be extreme.

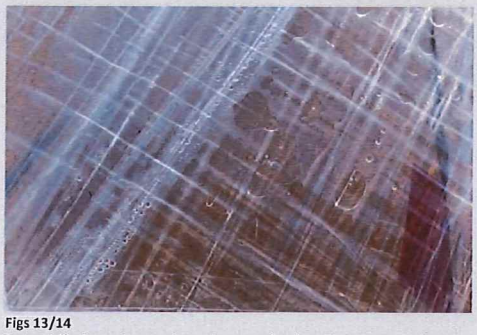
For this reason, the Tyvek® Xtreme™ W50 cover qualification programme investigated this by incorporating a solar exposure period during three days after the test pallets had arrived in Luxembourg. Ambient temperatures were cool and dropped to freezing point at night, but with clear skies during the daytime it was possible to test the effectiveness of the reflective Tyvek® covers at low ambient temperatures.

Fig 12

EXTERNAL EXPOSURE TRIALS: Pallet Top Temperatures

9 **LUXEMBOURG 26/02 - 29/02**





Figs 13/14
Potentially damaging condensation was clearly evident beneath the impermeable film cover

Figs 15
The micro-structure of Tyvek® permits the escape of damaging water vapour

OTHER OBSERVATIONS

Condensation

An appreciable volume of water was evident underneath the comparative stretch-wrap film cover after the pallets had been subject to cold ambient conditions. Since the physical phenomenon of condensation is inevitable with impermeable materials when subject to hot/cold cycling in humid conditions it is expected that this phenomenon will inevitably affect all non-breathable covers The measurement of condensation formation was not part of the qualification exercise.

Damage

An inspection of the Tyvek® Xtreme™ W50 covers at the conclusion of the exercise found that there was no damage to either the inside or outside of the covers as a result of handling and transportation. Some cover materials are susceptible to handling damage such as abrasion and penetration which can compromise the protection afforded.

CONCLUSIONS

The results of the Tyvek® Xtreme™ W50 qualification exercise proves conclusively that when used in accordance with the manufacturer's instructions, the cargo covers provide a significant improvement in product temperature stability and can be used with confidence to meet the current regulatory requirements for the temperature management of CRT pharmaceutical products.

APPENDIX A

Validation or Qualification?

Fig A.1

Much confusion surrounds the terms "Qualification" and "Validation" when it comes to good coolchain practice. The terms 'validation' and 'qualification' are often used interchangeably and both relate, essentially, to the process of proving that a process or equipment is 'fit for purpose'. Certainly the most important thing of all is to ensure that something is fit for purpose rather than get bogged down in semantics.

However, the International Conference on Harmonisation (ICH) provides the following definitions* which are mirrored in the latest EU GDP guideline**:

Qualification

The action of proving and documenting that equipment or ancillary systems are properly installed, work correctly, and actually lead to the expected results. Qualification is part of validation, but the individual qualification steps alone do not constitute process validation.

Validation

A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined acceptance criteria.

What this means in practice is that all components or equipment used in a 'validated' coolchain must be individually 'qualified'.

The scope and extent of the necessary qualification steps should be determined using a documented risk-assessment approach.

So a product such as a Tyvek® Cargo Cover needs to be qualified to show:

1. that it consistently meets its quality and design-performance specification - thermal properties, breathability, strength, etc. (Operational Qualification); and

2. that it meets its performance specification under controlled conditions to demonstrate its performance behaviour in changeable, real life situations (Performance Qualification).

These component qualification exercises are normally carried out by the product manufacturer i.e. DuPont in the case of Tyvek® Cargo Covers. This qualification exercise will normally include an overall analysis of all the relevant elements and procedures of the distribution chain - route, handling, aircraft, airport facilities etc. followed by static 'worst case' tests and, lastly, by an empirical 'in-situ' service analysis where the outcomes are benchmarked against the static results.

This product qualification then forms part of the overall validation of a shipping route or other coolchain solution. These route validation exercises are normally carried out by the pharma company and/or its 3PL partners.

*International Conference on Harmonisation (ICH) Good Manufacturing Practice Q7 2000
**EU Guidelines on Good Distribution Practice of medicinal products for human use (2013/C 343/01)

About Cool Chain Component Qualification

With the manufacture of pharmaceuticals now a global industry and with the new EU GDP and other regulated quality control measures in place, there is a critical need for a structured and stringent validation of the components and solutions used in the transport of pharmaceutical products.

One area of particular concern is that of Controlled Room Temperature (CRT) logistics, otherwise known as controlled ambient temperature. The nominal CRT temperature band of 15°C to 25°C covers a large proportion of the finished pharmaceuticals that are transported across the world and for this there is a pressing need to put in place CRT management systems that are dependable, effective and affordable.

The regulations governing CRT storage and transportation basically require pharmaceutical companies and their distribution partners to take the appropriate validation and qualification measures to demonstrate cool-chain component and system performance and regulatory compliance. The difference between qualification and validation is often confused (see Appendix A 'Validation or Qualification') but in essence they are analogous terms relating to the evidential assurances required as part of a quality management system (QMS) governing the protection of pharmaceutical products during their transport to market.

GDP COMPLIANCE

To bring certainty, consistency and control to the often tangled web of outsource parties involved in pharma distribution requires a cool-chain strategy that embraces proven, reliable, thermal-protective technology. With much of the post-production life-cycle of a pharmaceutical product being being literally out of the hands of the manufacturer, it is essential that rigorous carrier and 3PL qualification systems are in place throughout the distribution chain as part of an overall cool-chain qualification programme.

To achieve this, the protective component parts and systems used during physical distribution must be suitably qualified and an appropriate control and monitoring programme put into effect covering all the possible conditions that might be encountered during each stage of transportation. Together with other key elements such as dependable tracking systems and certified operative training, a major part of any such a strategy relates to the specification, selection and validation of the discrete cool-chain components, equipment and systems that are brought together to form an overall 'qualified shipping lane' or 'GDP compliant' logistical solution.

COOL-CHAIN ROUTE QUALIFICATION - WHY IT'S NEEDED

Regulatory obligations make it necessary for producers to validate cool chains and qualify their associated shipping lanes to demonstrate that the necessary

controls are in place to ensure product and, ultimately, patient safety.

This means that all cool-chain packaging systems, vehicles and storage facilities, together with all attendant methodologies and operating procedures, need to be approved and performance-validated through a rigorous programme of pre-testing, field trials and ongoing data capture.

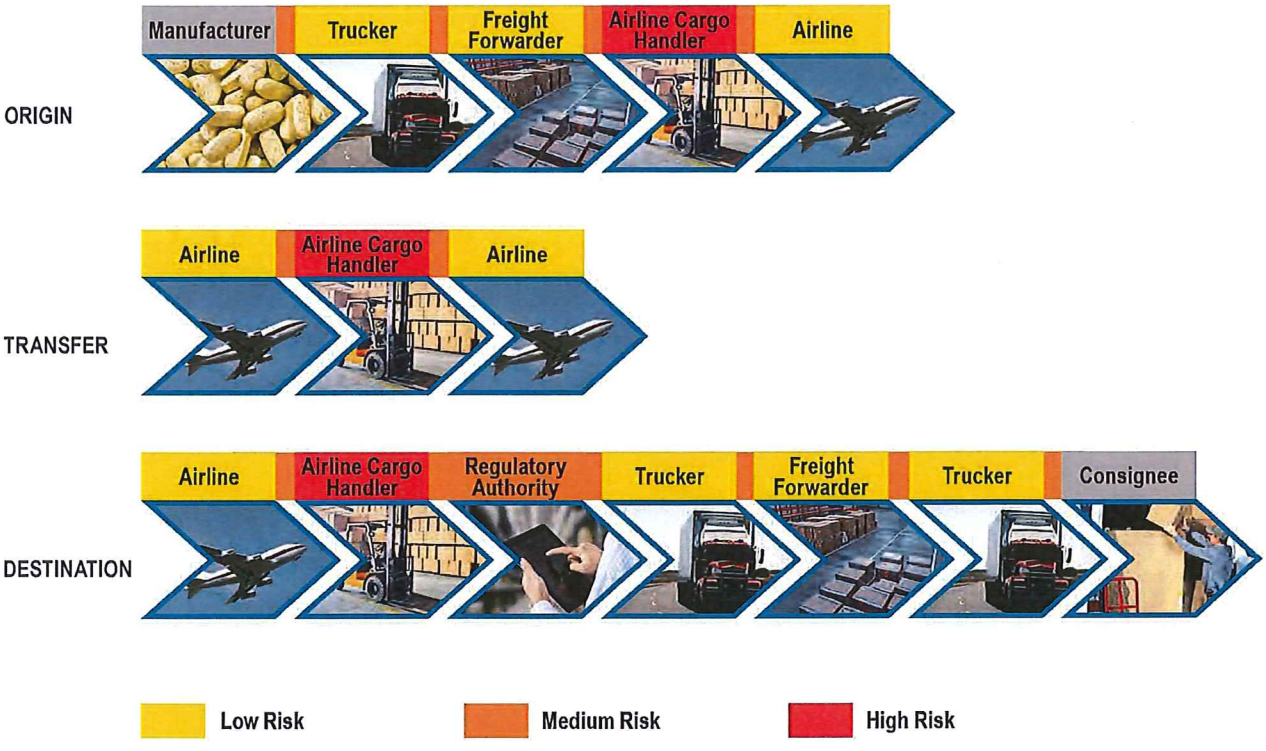
Transportation validation is part of the overall pharmaceutical quality control process. It is essentially a systematic approach to collecting and analysing the necessary data to give reasonable assurance and documented evidence that a specified cool-chain system and protocol will consistently operate as expected within specified parameters.

Weak Links

There are a number of recognised weak links in the pharma cool chain (Fig B.1). Moving pharma products from A to B has the potential to affect the efficacy and quality of a product or even to render it ineffective or, at worst, dangerous, so it is is important that adequate controls are in place to control risk.

Pharma producers bear a heavy responsibility, both legal and moral, to enact and enforce the most appropriate control measures during the shipping stages of the product life cycle. It is a responsibility which cannot simply be abrogated by transferring it along the supply chain and any organisation that neglects product safety is in breach of the law and taking an unacceptable gamble on both its own future and on the safety of the public.

TEMPERATURE EXCURSIONS - WHERE THEY OCCUR **Fig B.1**



By specifying the service levels required from 3PLs and by participating in key component validations and the development of qualified shipping routes, a pharmaceutical company is able to exercise control of its transport lanes and provide documented evidence that its products are being maintained within acceptable temperature limits throughout their entire journey from factory to pharmacy.

Critical Control Points

In establishing these controls the prevailing laws around GDP provide guidance to pharma companies. However, they are not prescriptive. It is down to the manufacturer, usually in partnership with its logistics partners and component suppliers, to develop and test the appropriate validation measures necessary to prove that their distribution arrangements are under control and 'fit for purpose'. In other words, transport validation has to cover the entire pharma distribution process inclusive of all third party involvements.

This involves establishing the critical control points in the distribution chain and qualifying each individual step. It is a process that must embrace the entire mix of methods and Standard Operating Procedures relating to personnel, equipment, packaging, transport, storage, measurement, monitoring and recording.

Steps

The individual control steps are developed, tested and documented (**qualification**) followed by testing and documentation of the resulting end-to-end process (**validation**). The resulting cool-chain system with all its component products, processes and procedures must then be actively monitored in use (**verification**) to ensure it remains relevant to changing operating and environmental conditions.

Cool-chain Product Qualification

When it comes to the individual components that are used to manage temperature sensitive products in a cool chain, Product Qualification is achieved by subjecting the equipment to two different types of test; fully controlled static tests (**Operational Qualification or 'OQ'**) and dynamic 'in-use' tests (**Performance Qualification or 'PQ'**).

In the case of OQ, this step is conducted under both 'normal' and 'worst-case' environmental conditions to determine the operational parameters of the individual components and to evaluate how they function as part of an overall cool chain system. The overall objective is to control the variations that result from the predictable interplay of all the known cool-chain elements in order to ensure pharma product quality and patient safety.

Both OQ and PQ elements of the Product Qualification feed into an overall Transport Validation which, in turn, will typically form part of a manufacturer's overall GDP Process Validation Plan (see Fig B.2)

Operational Qualification

Designed to explore and document the functional envelope for a cool-chain component, Operational Qualification (OQ) tests are a vital part of the

qualification programme. The OQ tests evaluate the correct functioning of the cool-chain components under both the expected and extreme operating conditions that have been identified in a comprehensive GDP risk analysis. Such an analysis includes the identification of hazards and the analysis and evaluation of all risks associated with exposure to those hazards.

This preliminary risk analysis therefore establishes the technical parameters of the component's performance, i.e. its ability to meet or exceed reasonably expected worst-case operating conditions, together with its operating limits.

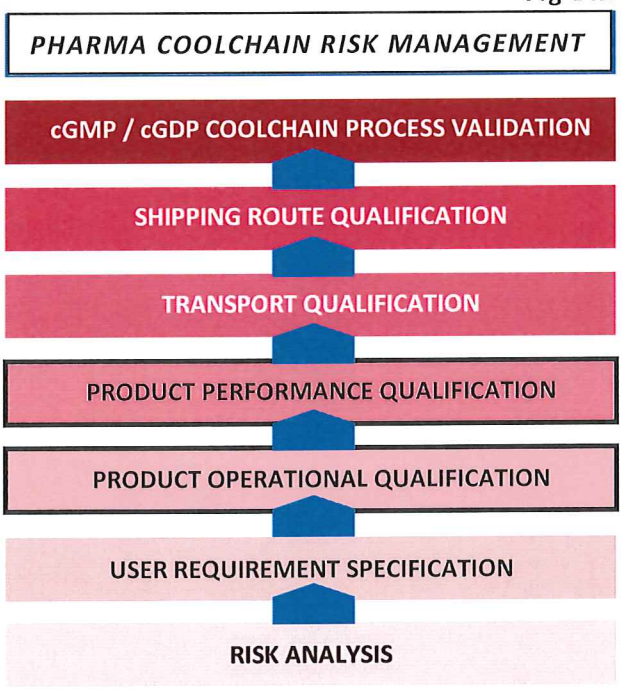
In the case of a cool-chain component such as a cargo cover, this preliminary risk analysis must consider all the potential variables at play. For example, with a thermal cover such as DuPont Tyvek®, the OQ testing needs to consider not only the effects of ambient temperature extremes, but also the importance of solar radiation and its related effects on the potential temperatures experienced by pharma merchandise in transit.

It is essential that this risk analysis is rigorous and thorough because, if and when an unacceptable temperature violation occurs, it will be necessary to demonstrate that the qualification process was appropriate to the risks under consideration.

Pre-Qualification

In some lower-risk cases, OQ tests results may be deemed sufficient to 'pre-qualify' a cool-chain component product for 'off-the-shelf' operational use. These 'one-size fit all' solutions reduce costs and save time and for some specific needs can be appropriate. A situation where pre-qualified cool-chain components might be considered appropriate, for example, might involve a regular short-haul route within a single climatic zone using a reliable logistics partner and with a known coolchain infrastructure at journey start and end.

Fig B.2



However, a reliance on 'pre-qualified' component products brings its own risks and can lead to protection for temperature-sensitive pharma merchandise that is either under- or over-specified for a given use or situation. Operating conditions can vary enormously even within a given shipping lane.

Environmental extremes, different pharma merchandise characteristics and densities, changing loading patterns, varying payload sizes etc. are just some of

the factors that can easily lead to 'out of spec' conditions. Similarly, 'pre-qualified' status is of very little value when it comes to the selection of cool-chain components since it confers no recognised standard of quality or performance and there are no normalised test regimes to enable like-for-like comparisons between competing cool-chain component products.

Performance Qualification

The Performance Qualification (PQ) determines that both a cool-chain component's specified performance and the results from its OQ are achieved consistently when the component forms part of an overall cool-chain protocol.

The purpose of the PQ is to verify and document that the cool-chain component concerned is functioning correctly and reproducibly within the entire specified working range and limits i.e. its 'fitness for purpose'. Therefore, for PQ purposes the component is always tested as part of an overall cool-chain process or process step. This requires the PQ stage to be based around field studies demonstrating how the component performs under actual conditions of use.

However, it must be clear that the PQ part of a transport qualification is designed to demonstrate that the component will function as expected under normal operating conditions. It is not intended as a test against environmental extremes, which by their very nature are unexpected and unpredictable events and consequently cannot be planned for and built into this part of the qualification.

Verification - Repeatability & Consistency

Transport GDP verification involves conducting several repetitions of a validated solution to confirm its efficacy and consistency in the field. Verification then continues as an ongoing process which is carried out continuously or periodically while the component product remains 'in-service' to ensure that it remains appropriate and effective in use and to accommodate planned and unplanned changes that may occur in the distribution chain. In this respect, a clearly defined change control policy must be in place and the principles of corrective and preventive actions (CAPA) applied wherever necessary.

Verification also identifies opportunities for new and upgraded component products and procedures to be introduced. In real-life situations, of course, a need for these adjustments may not become apparent until an acceptable temperature deviation occurs. A system must be in place to ensure that any such excursions are not only recorded but are brought to the attention of the appropriate quality management.

Summary

The latest EU Good Distribution Practice has extended regulatory measures to cover the CRT temperature band and, at a stroke this has substantially increased the volume of pharma products that are now within regulatory scope. Most pharmaceutical merchandise requires storage and transportation at ambient temperature and a failure to take fully validated thermal protection measures could have catastrophic consequences for both product and patients.

DuPont™Tyvek® Cargo Covers Distributor

QRWAYBILL Sàrl
17, route du Marais, door 46
CH-1860 Aigle
Switzerland

Contact Walter Richner
Phone +41 79 446 2988
Mail exec@qrwaybill.com

Tyvek. cargo covers