MEDICAL ENGINEERING TECHNOLOGIES

GLOBAL EXCELLENCE IN DEVICE TESTING

VERIFICATION OF INJECTABLES IN TRANSPORT AND STORAGE

Here, Mark Turner, Managing Director, Medical Engineering Technologies, discusses the regulations and requirements around testing combination products for their stability in storage over their shelf-life and during transport.

INTRODUCTION

From the May 26th, 2021, many combination products will be included in the EU Medical Device Regulation (2017/745), commonly known as the MDR.[1] Specifically this inclusion is by Article 117 of the regulation. If your delivery device is a single integral product, including the drug, that cannot be reused, it must comply with the medical device General and Safety Performance Requirements (GSPRs).[2] These requirements include verification of the device's robustness in storage and transport.

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STABILITY REQUIREMENTS

Pharmaceutical companies are familiar with the use of ICH guidelines[3] when demonstrating the stability of their formulations. The storage conditions outlined therein can be used for preparing combination products for performance testing at various points throughout their safe storage period, which is often the case in practice. For example, a dose accuracy study for a biosimilar injection will use a product that has been stored at the normal 4–8°C because the product, or other components of the formulation, could denature or degrade at 25°C and thus alter the measured dose dispensed.

"This standard allows the use of accelerated ageing to obtain packaging stability information, in advance of waiting for natural ageing to produce test material that has completed its recommended storage period. This is acceptable for both the secondary packaging and the CCIT."

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From the medical device point of view, the syringe is the sterile barrier packaging (GSPR 11.4).

This, for the syringe needle cover and stopper joints, would require a closed container integrity test (CCIT), an example of which can be seen in Figure 1.[4] If the combination product has secondary sterile barrier packaging, there will often be a blister or a pouch pack. Both the syringe seals and any secondary packaging will be subject to ISO 11607 Part 1 as part of the GSPRs.[5] This standard allows the use of accelerated ageing to obtain packaging stability information, in advance of waiting for natural ageing to produce test material that has completed its recommended storage period. This is acceptable for both the secondary packaging and the CCIT. A temperature of 25°C is acceptable for this accelerated ageing. Typically, the rapid ageing for a medical device is carried out at 55°C (a condition that is not found in the ICH guidelines). At this temperature, for a product that is normally stored at 4–8°C, an equivalent shelf life of three years would be attained in approximately six weeks (ASTM F1980).[6] This allows the stability of the packaging to be validated well in advance of the validation of formulation-related performance aspects.

"With regard to the formulation, arctic or desert conditions are likely to be the most severe. When thinking about the carton, tropical (38°C/75% relative humidity) is usually the most severe environment."

Figure 1: Closed container integrity testing using a trace gas technique.

Figure 2: Air bubble movement measurement in simulated air transport.

TRANSPORT REQUIREMENTS

ISO 11607 also requires confirmation of the combination product's robustness in transportation. The specific standard used for this is usually ASTM D41697.[7] This standard gives conditioning (input) recommendations to simulate transit. These include stacking, concentrated impact, vibration and manual handling. There are a variety of pre-conditioning atmospheres that need to be applied, usually for 72 hours, before subjecting a shipping carton to the transit inputs. These would not be relevant for a cold-chain product.

For a device that is shipped without temperature control, consideration must be made of environments into which a carton may be shipped. With regard to the formulation, arctic or desert conditions are likely to be the most severe. When thinking about the carton, tropical (38°C/75% relative humidity) is usually the most severe environment. Other situations should also be considered, the most common one for delivery devices being air transport. For example, it is possible that an air bubble inside a prefilled syringe would expand and contract as an aircraft changes altitude. This can cause movement of the fluid, which in turn might cause a change in the dose available, or lead to evaporation and the deposit of residue which could block the needle aperture. These effects can be simulated in an air transit test chamber (Figure 2).

CONCLUSION

Drug-device combination products are just that, multi-component systems which straddle the medicinal and medical device regulatory systems. When it comes to stability testing, both pathways must be followed to demonstrate the stability of the formulation and of the packaging

components. For the resistance to damage in transit, the two pathways largely overlap with consideration included for any product-specific hazards that have been identified in a risk analysis.

ABOUT THE COMPANY

Medical Engineering Technologies (MET) has successfully delivered design validation testing to medical device and pharmaceutical companies in 20 countries across Africa, Asia, Australasia, Europe and North America. MET knowledgeably, reliably and effectively delivers medical device and packaging testing. Services include protocol development, laboratory testing and data analysis. The laboratory is equipped for performance testing, chemical analyses and sterile barrier verification and – with accreditation to ISO 17025 – customers can have complete confidence in the quality and accuracy of results.

REFERENCES

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ABOUT THE AUTHOR

Mark Turner is Managing Director of Medical Engineering Technologies, which provides a wide range of services to engineers and project managers in the medical device industry. Mr Turner founded MET in 1997 after 12 years of project management and device design with Smiths Medical. He has also worked as a perfusionist in the cardiac unit of Kings College Hospital, London, UK, providing experience of the application of medical devices first-hand. He received a BSc in Chemistry (with Biochemistry) from the University of Wales (UK) in 1983 and has also studied astronomy, business administration, cosmology and opto-electronics.

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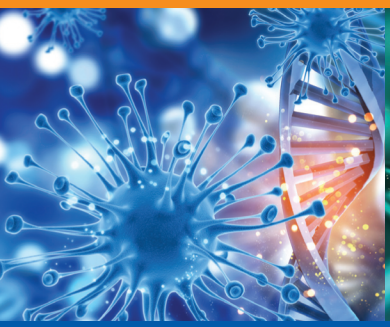


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