The Impact of the GDP Guidelines on Design, Qualification and Validation of Packaging Systems

PEER REVIEWED

It was nearly a month to the day after I presented to a life science audience in Shanghai, China that I found myself before another set of life sciences industry professionals in Galway, Ireland. I was asked to address the impact of the new EU GDP Guidelines on design, qualification and validation of packaging systems.

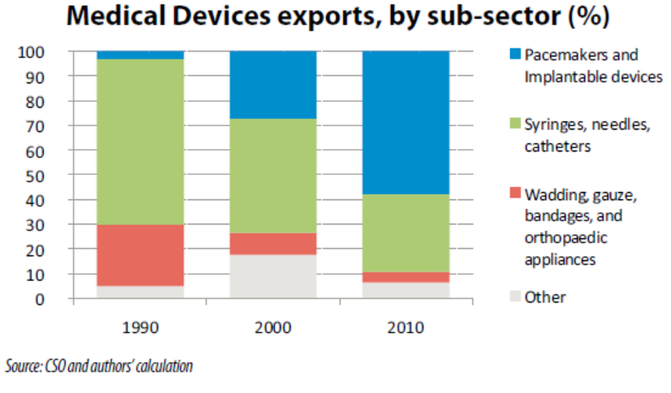
As I said to the audience, "Over the last 15 years I have presented and talked in most regions of the world, however it's always the case that the home crowd is the one audience that strikes the fear of God into you, so if you see me develop rabbit headlight eyes you will know where I am coming from."

I talked about the importance of the life sciences industry in Ireland and what a valuable asset it is to the overall economy. According to the IDA Ireland, nine of the top 10 pharmaceutical companies have a location in Ireland and it was the fifth largest exporter of pharmaceuticals in the world in 2012 .

Medical devices exports also helped drive Ireland to be the largest exporter of both pacemakers and other implantable devices in 2013. Medical devices exports increased by an average of 14% per year from 2008-2012 according to the IEA Top 250 Exporters Report 2013. Exports in pharmaceuticals and medical devices totaled €56.5 billion. "The reality check is that 80% of medical devices firms operating in Ireland were foreign-owned multinationals in 2011," I told the audience.

We all know that some of the initial factors encouraging direct foreign investment were a favourable tax situation, and a young, educated, English-speaking workforce. These have benefitted many businesses which have chosen to have a location in Ireland.

Two colleagues were recently consulted on the subject of GDP for an article in another publication. The European Head of Technical Services provided a scientific/technical point of view, while Stephen Healy, Global Director of Sales, looked at the business development side. They debated a number of crucial questions.



Source: CSO and authors' calculation

As was pointed out in the article, the new European Union (EU) Guidelines for Good Distribution Practices (GDP) do not seem to be a very interesting subject on the surface. However, if one looks a little deeper, it is a subject which affects all of us. As I said in my presentation, "I assume everyone in this room takes an over-the-counter medicine or has a family member who does. Who doesn't? This is why the new rules are so very important to everyone."

How do the guidelines approach this issue? By using risk-based methodologies to evaluate the integrity of the supply chain. The bottom line is patient safety. These methodologies have two main goals within the supply chain: reduce the risk of drug damage by environmental exposure, and reduce counterfeiting.

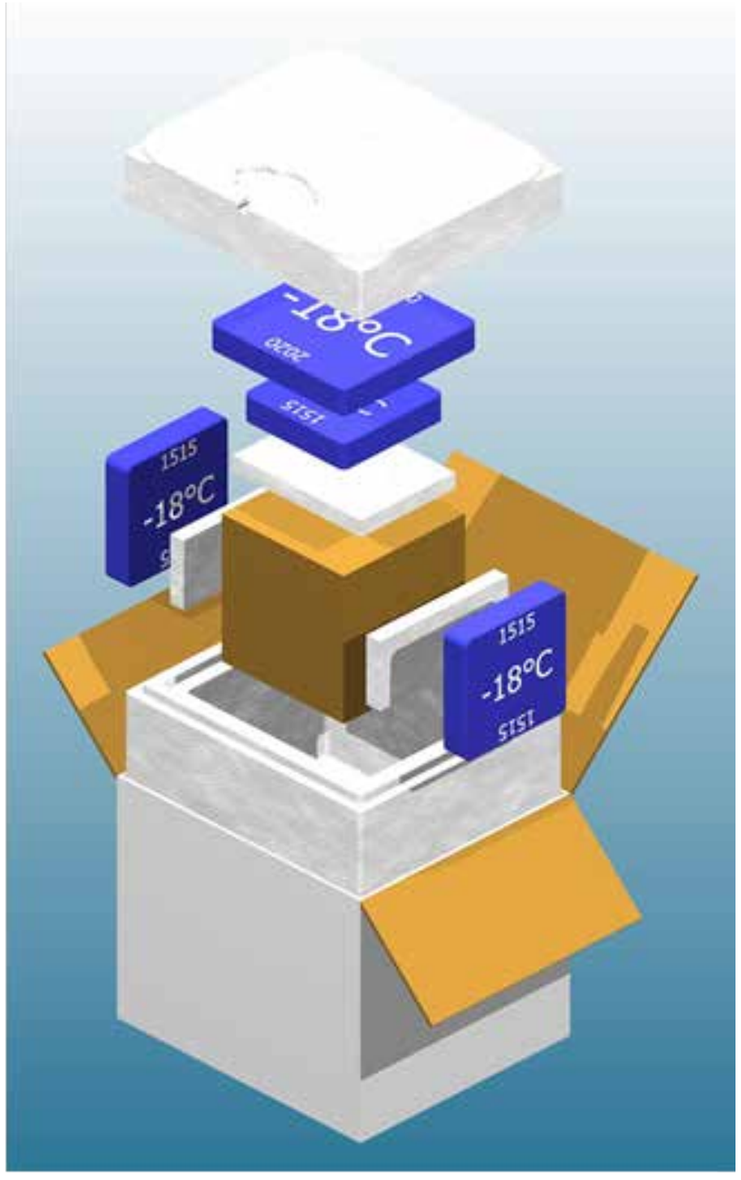
Drugs can be damaged by adverse external exposures and thus lose efficacy or become toxic, even deadly. "Obviously a key area that affects drugs is temperature exposure. Temperature-related damage to drugs is not readily visible and can occur at any point in the supply chain. The guidelines are designed so that a product not just makes it to the doctor's office or pharmacy but is maintained at the appropriate temperature throughout its journey to ensure its safety and efficacy when it reaches the patient," I said.

For those in the audience who hadn't examined the guidelines closely, I gave the 10 chapter titles for the specific areas they address.

- Quality Management
- Personnel
- Premises and Equipment
- Documentation
- Operations
- Complaints, Returns, Suspected Falsified Medicinal Products and Medicinal Product Recalls
- Contract Operations
- Self-Inspections
- Transportation
- Specific Provisions for Brokers

While some areas being refined contain as few as four separate guidelines, chapters on operations and transportation each contain more than 20 separate guidelines. The bottom line is that improving standards will bring significant changes to keep pharmaceuticals and other medications safe throughout the supply chain and ultimately reduce the risks for the people who use them.

There are two chapters of the guidelines that mention specific requirements for temperature control. In the premises and equipment area there are 29 separate guidelines. From a record-keeping and auditing perspective, these activities need to be recorded and documented in a robust way; an example would be to ensure records are in compliance to 21CFR Part 11 which covers data integrity. The same guideline then talks about qualification and validation. Those terms mean something a little different to those of us in temperature-controlled packaging, but we'll get in to that later. The guideline states: Suitable equipment and procedures should be in place to check that the environment where medicinal products are stored is suitable and that storage areas should be temperature mapped and monitored.



"Maintaining appropriate temperature of pharmaceuticals or biological samples during their transportation from the laboratory or manufacturer to the patient is what we do every day," I said.

In chapter nine there are 23 separate guidelines addressing the issue of protecting the products against breakage, adulteration and theft while utilising temperature control to maintain the product's quality. Specifically, "The required storage conditions for medicinal products should be maintained during transportation within the defined limits as described by the manufacturers or on the outer packaging." This includes medicines that are maintained between 15 and 25°C, like many OTC products. In addition, the guidelines state: "It is the responsibility of the wholesale distributor to ensure that vehicles and equipment used to distribute, store or handle medicinal products are suitable for their use and appropriately equipped to prevent exposure of the products to conditions that could affect their quality and packaging integrity."

What does this mean in practice? It means that you have to ensure that your packaging systems or devices

are properly qualified and validated. Qualification is what we refer to as an individual quality staged process which combined (DQ-PQ-OQ) will lead to adoption of the qualified system into an organisation's validation plan.

Explicit implication is that your supply chain requires qualification and validation. This by default includes the packaging used and how you use it. This must be evidenced by way of suitable data and should take into account possible delays or changes to routes when being validated.

The guidelines stress the need for using properly qualified thermal control systems. "For temperature-sensitive products, qualified equipment (e.g. thermal packaging, temperature-controlled containers or temperature-controlled vehicles) should be used to ensure correct transport conditions are maintained between the manufacturer, wholesale distributor and customer."

As the guideline is written; "If temperature-controlled vehicles are used, the temperature monitoring equipment used during transport should be maintained and calibrated at regular intervals. Temperature mapping under representative conditions should be carried out and should take into account seasonal variations."

As I said, "These are new and specific requirements which will have a direct impact on what you currently use and what you may have to move towards if you need to upgrade your packaging systems. Cold shock is a serious issue and an indirect target of these guidelines is to reduce drug and vaccine spoilage and degradation. One way we solve this issue is by moving away from water-based coolants to other phase change materials to effectively eliminate this risk.

"Packaging performance is entirely at the mercy of the 'conditioners', otherwise known as your staff who prepare and pack out passive packaging systems. They are now required to have professional training on preparing and conditioning of coolants to ensure performance of your validated systems," I stated. Training and SOPs are keys to ensuring best practices are observed and followed.

Issues around cold shock prevention and coolant preparations and handling are addressed in the guidelines as follows: "If cool packs are used in insulated boxes, they need to be located such that the product does not come in direct contact with the cool pack. Staff must be trained on the procedures for assembly of the insulated boxes (seasonal configurations) and on the reuse of cool packs. There should be a system in place to control the reuse of cool packs to ensure that incompletely cooled packs are not used in error. There should be adequate physical segregation between frozen and chilled ice packs."

You may need to re-engineer current systems to include a payload protection carton or some other way of protecting the payload from direct exposure to frozen components. Again, if your components are not conditioned properly then underperformance will occur. Understanding the thermal and time challenges drugs will experience is critical to making an informed decision as to how to protect them against degradation. Implementing these guidelines will increase the quality of the product at the patient end. This is the part of the chain that matters most. As we have seen with GMP and good clinical practice, improving standards brings more effective treatments to more patients. GDP will tighten the controls and enhance the chances that a patient, relative or friend receives a treatment that works as expected, outcomes we should all expect to be delivered.

David P. Walsh, Founder & Chief Executive Officer. David Walsh founded DGP Life Science in 1998 after co-launching and running the dangerous goods packing company, Trident Safety Group for ten years. Since then, Mr Walsh built the DGP Headquarters and Research and Development Center in the United Kingdom and expanded its manufacturing facilities from the UK to the United States, Ireland, The Netherlands, India, and Malaysia. To reflect the focus and the growth of the life sciences packaging business Mr Walsh rebranded the life science packaging division in 2011 as Intelsius, A DGP Company. Mr Walsh has extensive knowledge of clinical trial logistics, the pharmaceutical cold chain, dangerous goods legislation and compliance. The combination of skills and experience make him an invaluable asset both to Intelsius and its clients. His commitment to green solutions development sets him apart from traditional entrepreneurs. Mr Walsh has many published articles to his credit; "The Five Steps of Contingency Planning" was published in the November 2012 issue of another trade publication.