IQPC Presents ...

Pharma Logistics IQ

This resource booklet will give you a flavour for the things to expect from Pharma Logistics IQ

Pharma Logistics IQ

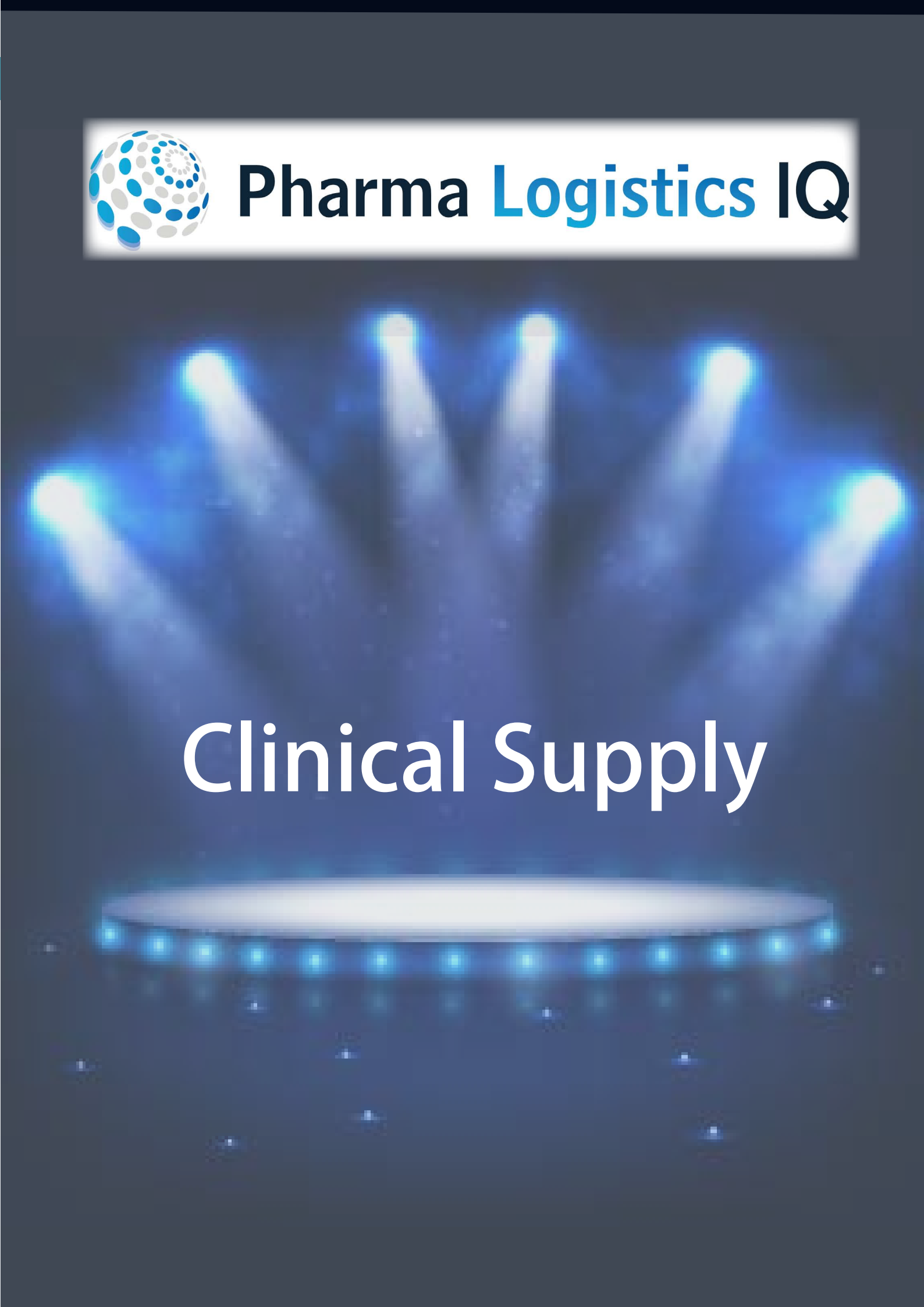
What to expect from Pharma Logistics IQ

For the last four years, Cold Chain IQ has acted as an international resource center for temperature control life science professionals, delivering insightful, unbiased information about the latest 'hot topics'. The portal focused on all areas of temperature controlled logistics, distribution and quality in pharmaceuticals and biotechnology. While maintaining one of the largest cool chain pharmaceutical international databases the IQ has offered strategic partners, members and contributors an unparalleled opportunity to network, share ideas and disseminate best practice information across the globe with peers within a collection of online events and webinars.

Now, the makers of Cold Chain IQ and Pharma IQ bring you Pharma Logistics IQ, dedicated to end- to-end excellence. The new portal will continue the work of Cold Chain IQ remaining devoted to the temperature controlled logistics sectors and its temperature controlled logistics memberbase but also looking to extend its reach to neighboring areas of pharma logistics including, clinical supply, supply chain security, regulations and more. Essentially Pharma Logistics IQ works to assist the industry in optimizing the path from lab to patient via world-class resources and networking opportunities.

This e-book will provide an overview of the topics to expect to feature within the scope of Pharma Logistics IQ.

Contents- Pharma Logistics IQ


Pharma Logistics IQ
Clinical Supply

Clinical Trial Supply

Pharma iQ
a division of IQPC

Minimising Wastage in Time and Money

Clinical Trial Supply Europe

Clinical Trial Supply : Minimising Wastage in Time and Money

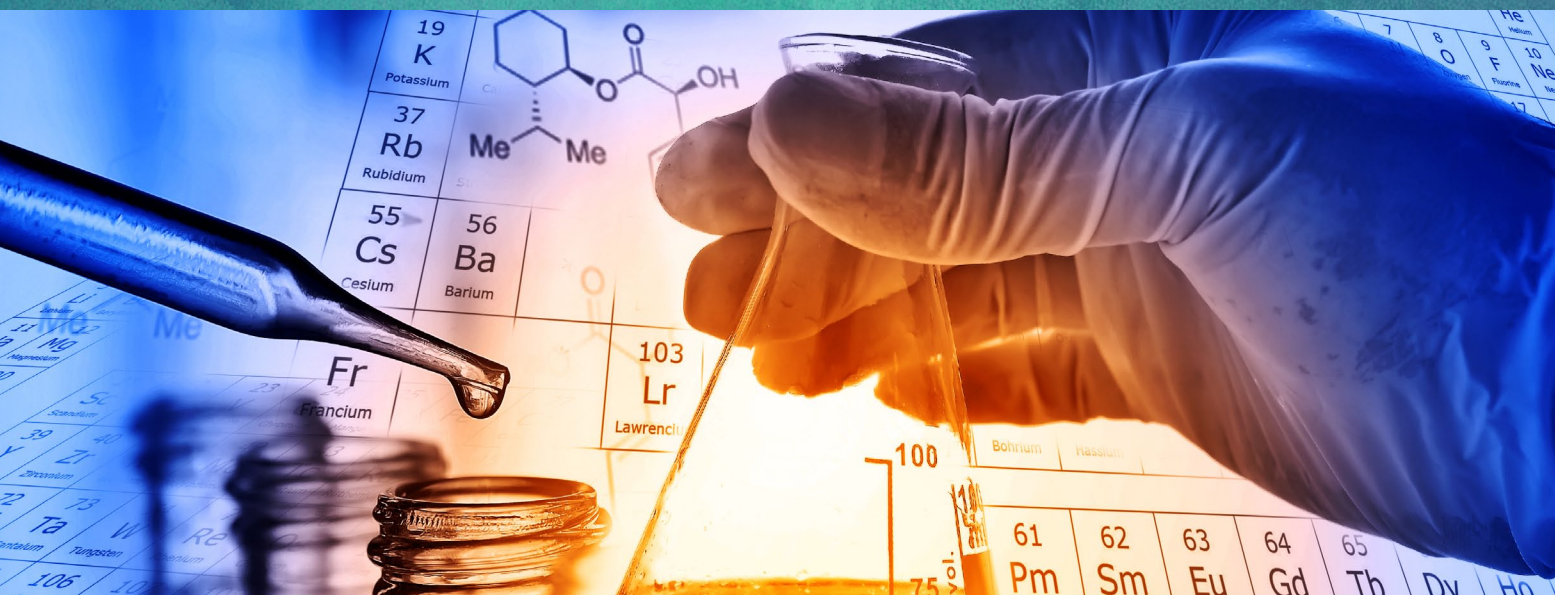
The operation of clinical trials are integral to the progression of the pharmaceutical industry. These trials can be orchestrated on a global scale, producing and distributing the drug in question to participants over several years.

Therefore, the supply of these trials represents one of the biggest challenges to be navigated. Undoubtedly, the efficient management of clinical trial supply entails regulating two dominant variables: time and money.

It is estimated that in total, it takes more than 15 years to develop, test and license a new drug and sometimes billions to fund the process. Badly budgeted or scheduled clinical trials can have the potential to severely hinder the progress made.

As a result of these considerations being of prime importance to the R&D industry, Pharma IQ discussed the concept with a clinical trial supply expert - Dr. Andrea Zobel Global Senior Portfolio Director Clinical Logistics at Parexel.

Best Wishes | Chanice Henry Pharma IQ Editor



Give us an idea of the worst case scenario if a firm doesn't take the right steps to minimise wastage?

"Looking at the drugs [themselves], the worst scenario is always that patients cannot be supplied, that we have to stop enrolment or even [enforce] a stop of the patient treatment."

In regards to controlling the use of funds, Andrea has seen cases where: "The budget was much [over the] expected budget , and this can lead to bankrupt a company - a sponsor company."

For example, when firms have not considered the payment or packaging of a concomitant medication which was not approved: "I've seen situations where the costs are increased enormously and in the area of millions."

Andrea also highlighted another pitfall can be encountered when enrolment data is not timely corrected and adapted:"… so drugs are purchased or produced [and] then they expire before they can even be used."

> " I've seen situations where costs are increased enormously and in the area of millions..."

What planning uncertainties can add hurdles to the process of avoiding wastefulness?

"The insufficient provision of data. Often an issue [is] that enrolment data is not updated in time and the information is not forwarded and [with] the site storage capacity, [so] we don't know what the site is able to store.

"Of course the production capacity is an important factor - that it's known if it's possible to provide, in a certain timeframe, the required amount of drugs.

How does temperature controlled logistics management impact requirements when minimising wastage?

"From [a] technical point of view, of course the shipment packaging must fit and must keep the required temperature. [It must maintain it for] the required time when you have, for example, an import-export process and the drug could [remain] in customs."

Andrea added that temperature excursions can cause costs in time, if a handover from shipment to site is not managed properly. Investigations into when and where the excursion occurred can lead to the site not being supplied properly within the required timeframe.

She continued: "The ideal situation would be to have an, automatic transfer of the temperature data, which automatically reads the data and releases it and there is no human influence necessary."

Your Golden rule to minimising time wastage in clinical trial supply

"The golden rule to minimise the

wastage in time in clinical trial supply is really the early involvement of the clinical trial supply unit. So that during collection of all study parameters this unit is involved and has the data available very early and can be involved in the study planning.

"For example, often the country selection, could be influenced by the clinical trial supplies unit and also to develop the protocol.

"The dispensing schedule can help a lot to optimize the distribution strategy and to avoid delays during execution.

"Sometimes there is a possibility in the dispensing schedule to provide some spare time from enrolment and randomisation up to drug dispensing

and that can help to support timely distribution and reduce overage. So their early involvement is really the key."

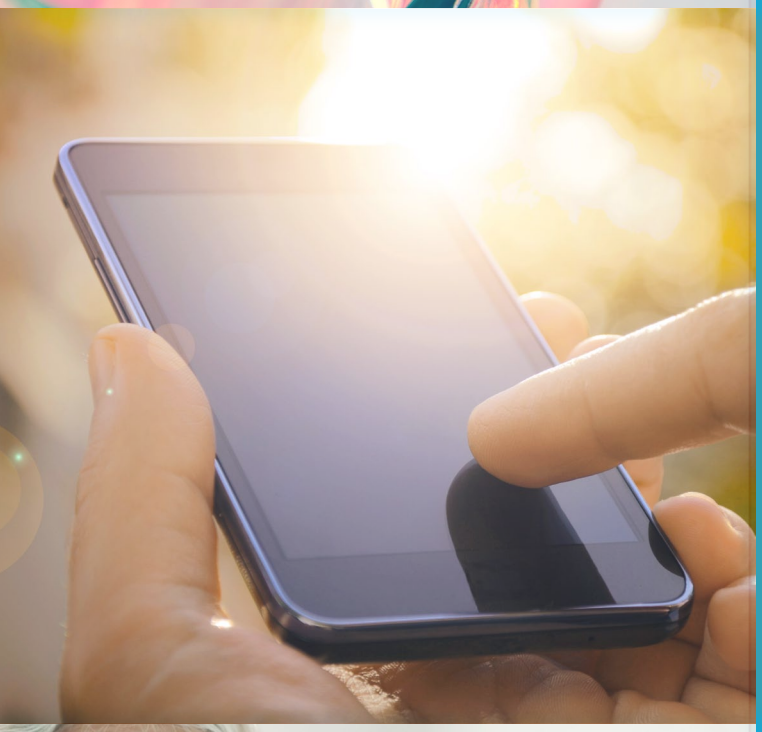
Your golden rule for minimising economic wastage in clinical trial supply

"The main strategy should be always to balance, and one of the important points is to balance the shipments against the overage so that [there is] a clear picture [of] the shipment cost versus the drug cost.

"So, for example, a high overage of a cheap product could lead at the end to an overall cost reduction, but this must be coupled from the beginning and with an overall picture.

"Another important factor is that the packaging of the drugs [should be] adapted to the whole supply chain. One example, the size should fit into the shipment packages. So ship drugs, not air."

The Clinical Trial Supply Summit will tackle many of the hurdles experienced in this area, turn over for more information.



Innovation in Clinical Trial Supply

Pharma iQ
a division of IQPC

Pharma iQ
a division of IQPC

Clinical Trial Supply Europe

Innovation In Clinical Trial Supply

Innovation is thought to be a keystone in the process of being competitive in any market. Within clinical trial supply, a lack of innovation can be costly in regards to a range of variables.

With this in mind, Pharma IQ discusses the latest trailblazing techniques in the arena with a panel of Clinical Trial Supply specialists.

Panel

Dr. Andrea Zobel
Global Senior Portfolio Director Clinical Logistics, Parexel.

Due to feature in Clinical Trial Supply Europe 2016:
- Expert Panel: Tracking Returns, Reconciliation & Destruction to Manage Costs
- Ideas Market: Exploring the Numerous Supply Chain Arms of Direct to Patient Shipments Session

Steve Jacobs
Board Chairman Global Clinical Supplies Group

Due to feature in Clinical Trial Supply Europe 2016 *As conference Chairman*

Bernard Jaucot
Associate Director Global Clinical Supplies PPD

Due to feature in Clinical Trial Supply Europe 2016:
- Expert Panel: Tracking Returns, Reconciliation & Destruction to Manage Costs
- Ideas Market: Exploring the Numerous Supply Chain Arms of Direct to Patient Shipments

Cedric Druck
Director, Belenox SPRL

Due to feature in Clinical Trial Supply Europe 2016:
Catch Cedric at the event in January for insightful discussion and networking.

The Consequences Of No Innovation

While contemplating the consequences of not innovating within clinical trial supply, the main factor highlighted was the loss of time.

Bernard noted: "We're at the end of the supply chain. We need to get those drugs as soon as possible on the market. So the more we win time, the more money they will win. For some blockbusters it's $1 mllion dollars a day, so you can understand the impact."

He adds that the ideal aim is to innovate so the industry can function faster while remaining compliant. He emphasises the need to interact with authorities so R&D firms can make smart adaptations and compliantly innovate.

"At the end of the day, a sick patient is waiting for this novel drug to make them healthier. If we don't do [things] correctly, he or she might die because of us …. So, yes, compliance is very important."

Andrea noted that a lack of innovation could cause focus on patient centricity to slip especially in regards to having the right patient recruitments. She indicated that the competitive environment will often provide the answer on whether initiative has slipped in this area.

Cedric noted: "Well, supposing that no innovation would take place, that would be an increasing challenge in the coming years for the pharma [industry] because drug development [has been] evolving in the past few years and the trend is continuing. So, more and more biotechnology, cell therapies and genome specific treatments are being utilized."

New research strategies such as adaptive trials, umbrella and bucket trials alongside the trend to obtain heightened analysis in less time both are placing pressure on the clinical supply industry.

In regards to these advances in trial design complexity, Cedric notes that the clinical supply chain needs to field these increasing levels of diversity via adopting new processes and methods. "….the fact of not innovating would really, I think, be a major hurdle in the coming years if pharma don't adapt their supply chain in advance."

Market Culture

As highlighted previously, the need for strict regulations has bred a what some dub as a conservative attitude towards innovation in clinical supply.

Bernard explained: "We have to work with standard, sturdy and robust, qualified processes, so that makes it, for me, a bit slower to really innovate." He added that he uses the term smart adaptation instead of innovation due to the idea that the market has to innovate in the open space that regulation has left available.

Steve said that due to the gradual approach to innovation or change, the industry's main issues have largely stayed the same. As the industry is risk averse by nature, a really clear return on investment must be evident for any new methods or techniques to be adopted.

Andrea noted that there is a tendency for the market to have rigid viewpoints – seeing each trial standing as a silo. She added: "They have a lot of potential to interconnect different trials by using technology and adapt this only with the client specifics... instead of having for each individual trial a complete new."

However, Cedric notes that innovation is one prevalent trend he has spotted within big pharma at the moment. Especially, in regards to making the supply chain more efficient and streamlined.

Recent innovative trends spotted within clinical trial supply include, interactive response technologies, planning and forecasting systems being connected to manufacturing and to the commercial supply chain and labelling strategies such as the decentralised just in time labelling,eLabelling.

eLabelling

One area of focus as of late is the concept of e-labelling - when the patent can access the labels virtually, so the physical box only holds a minimal aspect like a barcode that is linked to the e-label. However, specialists have highlighted that a recent potential directive has specified directions that go against the vision of e-labelling, by stating that all information including expiry dates must be shown on all labelling including on primary packaging.

In regards to these possible rules, Steve notes that this could produce hurdles for the market and enhance the reliance on methods such as just-in time labelling and on-demand shipping:"… versus where we were able to go ahead and … feed the site and put drugs there and then have all the other automation lines, the IRTs and some of the planning and forecasting go ahead and work for us."

He adds that some are hoping there will be a partial reversal upon the ruling on the clinical trial regulations on removing expiry dates.

Patient Centricity

Additionally, the shift towards patient centricity has triggered the existence of a range of fresh methods, including direct-to-patient

shipments, medical wearables connecting with smart phones and eDiaries

Bernard mentioned the possibility of using smartphones and tablet technology towards drug accountability and traceability. He added that that the potential from smart phones and tablets in the hands of investigators and patients could be: "Incredibly powerful for our business."

Pooling

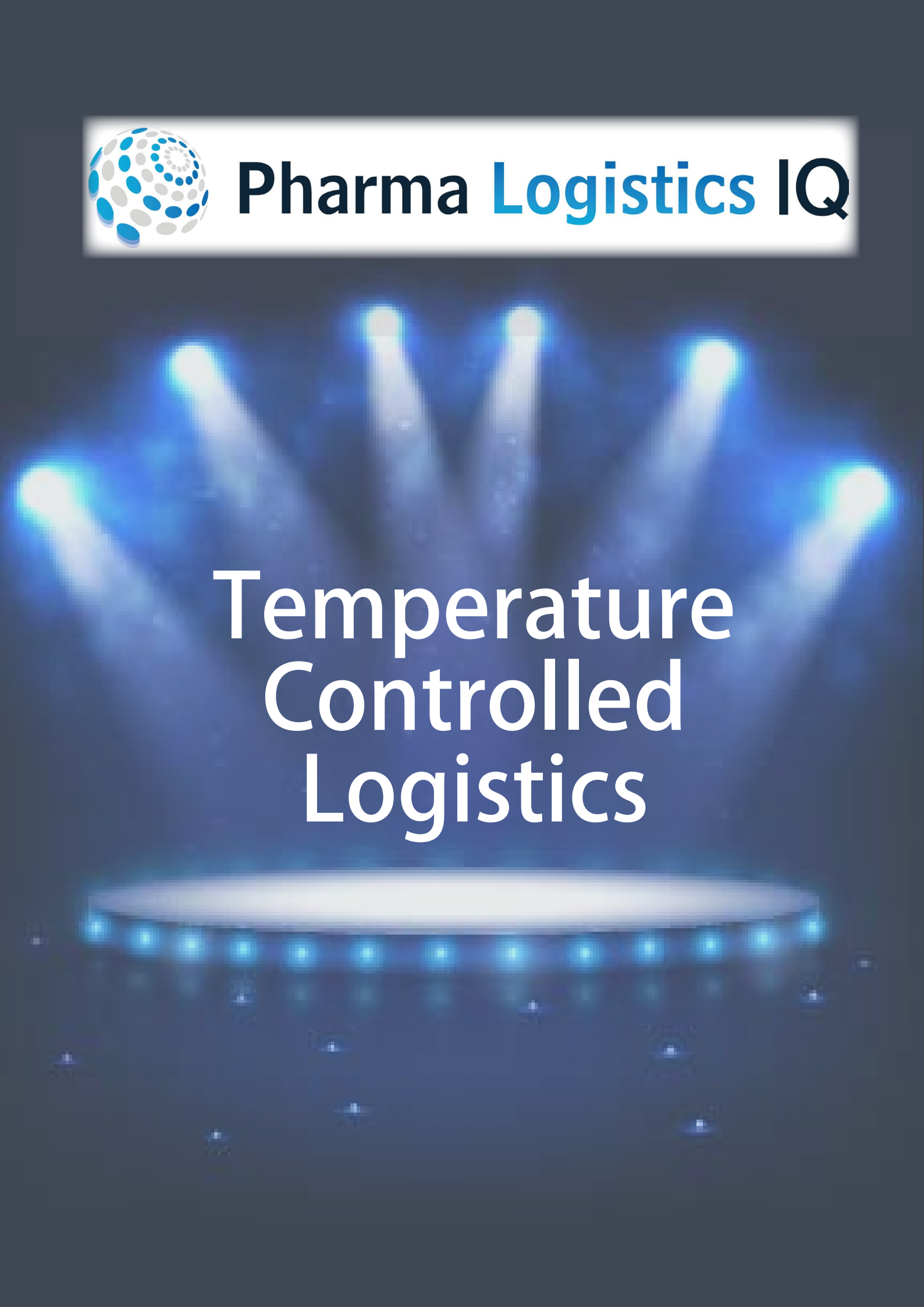
Cedric mentioned the development of pooling and adding several layers to the manufacturing in regards to transit. "An idea [being] to have some layers of intermediate products between drug product and secondary kits that can be pooled amongst trials and enable just-in-time labelling, just-in-time packaging."

Gaps in the Market

Andrea notes that the world of clinical supply could learn from the advances made in neighboring industries. "So when you are talking about tracking and tracing [for] pharma authentication, the pharma industry itself is far behind, for example, automotive or consumer goods, where they have such types of unique identifiers and theories. So, there is a lot of innovation potential by simply using what's already used in other industries."

When contemplating what needs to be on the horizon for clinical supplies, some in the industry feel that the market should play a more active role in sculpting policy and regulations with clinical development authorities. Others stressed a need to lobby to align the clinical trial supply industry with more commercial notions.

Clinical Trial Supply Europe's entirely interactive, discussion based agenda is due to address the burning issues today's industry faces.


Pharma Logistics IQ
Temperature Controlled Logistics

Optimising Airfreight

15TH ANNUAL COOL CHAIN
TEMPERATURE CONTROLLED LOGISTICS EUROPE

ColdChainIQ
Temperature Control Logistics & Quality Network

Optimising Airfreight

Airfreight as a service attracts a high price. But for products that warrant the costs of being transported via airfreight, this mode of transport is quick, supplies a high quality of service and can provide much needed compliance assistance.

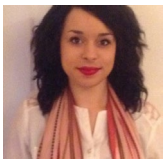
Life sciences products with a steady demand are better suited to be transported by ocean. However, David Bang, Global Head of DHL Temperature Management Solutions mentions that it is in line with the swift supply of new products where airfreight comes into its own.

"New products are constantly being introduced to new markets, which requires speed and flexibility based on smaller batch moves. The need for speed to the market and being able to accommodate fluctuating market demands will continue to rise no matter what."

He continued: "Speaking of the second advantage "regulatory compliance", over the last few years, the airfreight industry as a whole has stepped up to the plate to relieve some of the recent regulatory pressure that the life sciences & healthcare industry is facing, for example the EU GDP guidelines." In line with this focus on healthcare product handling on the rise, some freight forwarders have been aiming to obtain accreditations in this area from health authorities.

Products that are more temperature and time sensitive like biologics and biotechnologies are often more suited to airfreight rather than sea.

With this in mind, **Cold Chain IQ** has created this guide of elements to consider when optimising the use of airfreight within temperature controlled logistics.



Best Wishes | Chanice Henry - Cold Chain IQ Editor

Optimising Airfreight

Not All Services Will Be Suitable

Mark Edwards, Modalis notes that pharmaceutical services from airlines will vary from basic to comprehensive. "Basic might be asking the manufacturer to arrange their own protection with the airline merely monitoring the shipment whilst comprehensive might include active temperature control on the aircraft and the provision of multi-temperature ground handling warehousing." When determining which is the apt option for you, a thorough grasp on your product's needs under GDP is vital.

Mark adds: "You could then opt to temperature control across the whole route or perform a risk assessment and arrange transport on that basis. "Both options have their advantages and disadvantages. Full temperature control can add significantly to costs whilst a risk-based approach can lead to temperature excursions which tend to impact financially, operationally and reputationally."

Monitor All Shipments on Route

Mark recalled a recent situation he encountered which emphasized the importance of monitoring all transits on route.

"At a recent meeting with a pharma manufacturer, they stated that they did not experience any excursions during transport thus they employed no special precautions. Given the route their products were taking, this was a surprising statement. However, when they confirmed that they did not use temperature monitors, it soon became apparent why they had "no issues". The moral here is that all shipments should be monitored en route, whether that is by monitors you supply or using loggers built in to vehicles, aircraft etc is up to you."

Monitors supplied by the pharma or biotech firm on average are the easiest to manage. They enable swift and accurate decisions to be made on the back of their end to end data.

Airfreight Temperature Control Methods

Active shipping systems:

Extremely reliable but usually sits at the expensive end of the spectrum. Deployed in high value/ critical situations where a temperature excursion cannot be countenanced. The system provider should offer full support here.

Passive shipping systems:

Works very well when sufficiently set up and lane characteristics are fully understood. Requires no intervention and can be booked as regular airfreight.

Reliance on airline's own control systems

Mark reminds: "Airlines differ widely in what their "pharma service" offers so you should only go down this line if you fully understand what the airline is offering and where there may be gaps in their coverage; typically these gaps would be at the airline handling and ramp stages ie at the airport."

Optimising Airfreight

Use Data to Qualify Your Providers

Data generated by loggers can be utilized to temperature map, locate risk hotspots and play a key part in route or transport provider qualification.

"The use of loggers may highlight issues which you need to address [and] also an opportunity to qualify your providers and prove that they are doing a good job for you, thus confirming the validity of your risk assessments." Mark Edwards

Employ Complete Transparency Along The Supply Chain

The regulatory environment that surrounds the temperature controlled logistics industry is complex and ever evolving.

Governing guidelines exist to define the correct conduct for the transportation, documentation and security of pharmaceuticals, with varying country specific requirements. As a result, this forces a substantial level of communication between stakeholders in the chain from origin to destination to ensure swift and clean execution.

In line with the varying country specific requirements Tom Grubb, Manager, Cold Chain Strategy of American Airlines Cargo pinpoints:

"Canada, for example, has strict guidelines for pharmaceutical imports, as does Ireland, Brazil and numerous other countries. All of these regulations must be satisfied on the journey from pharmaceutical manufacturer to patient."

He adds: "Collectively, this is creating a rapid increase in the amount and type of regulatory oversight. While all these regulations are geared towards maintaining product integrity and patient safety, they also make moving temperature-sensitive cargo a complex, nuanced endeavour."

"Making the challenge more difficult still, regulations and requirements can conflict with one another and between stakeholders. Some stakeholders might even have different priorities and divergent understanding of what the regulations mean for fast, efficient cold chain transport. Addressing the differences between regulations and ensuring all stakeholders adhere to rules, while also achieving the speed and efficiency critical to the international pharmaceutical cold chain, demands collaboration."

"Pharmaceutical manufacturers, freight forwarders, air carriers and other stakeholders must have detailed conversations and group planning before a temperature-sensitive shipment

Optimising Airfreight

enters the cold chain. This means anticipating regulatory hurdles, agreeing on standards for documentation, understanding transfer times between flights and transportation modes, and adhering to all applicable rules – this while also delivering life-saving pharmaceuticals on time."

Avoid detriment from having multiple links in your air shipment

Tom Grubb notes: "On its journey, temperature-sensitive pharmaceuticals can cross different climate zones, encounter a range of threats to viability, and change hands between several forwarders, handlers, and even airlines. These and other conditions present potential threats to temperature-sensitive pharmaceuticals, and cold chain logistics partners must adhere to the myriad regulations designed to mitigate threats in transit."

An air shipment will feature a large amount of companies assisting with getting your product from end-to-end.

Mark notes that up to 27 companies may be involved, he continues: "This might seem excessive but think about it for a moment: you; the freight forwarder; the airline; the export Customs broker; the airline handling agent; the transport company which collects it and delivers to the airline; the ground handling company; Customs; regulatory agencies; etc – it soon adds up."

Nigel Wing, Global Head Life Sciences & Healthcare, DHL Global Forwarding, reminds: "At any point in the cold chain where product is passed to / handed over to another party, the risk increases. Reducing links and the handling involved in the chain is critical when assessing risk or likelihood of mistakes."

Mark suggests the adoption of of passive systems: due to their extra layer of protection, ability to work up to five days without intervention, although they do require careful preparation measures.

Clear delineation and articulation both internally and externally of your service requirements can manage these considerations. Remember to analyse your supply chain with an end to end perspective rather than limited INCO terms.

Conflicts of Interest

Some firms may choose to request temperature to be maintained between certain parameters via a declaration on the Airwaybill. Mark notes: " …but what if the majority of the cargo needs to be kept at a different temperature, or if the pilot uses degrees F instead of C or if, as is most common, your instruction is simply completely ignored?"

With this in mind, air freight volumes saw a rise at the start of this year. The International Air Transport Association (IATA) which represents 83% of total air traffic, charted a year on year increase at the start of 2015 in air freight volumes, which later dipped slightly in May. The trade association expects a sharp rise at the end of this year.

On the matter of conflicts of interest between freight orders on an airplane, Greg Giarratana National Airfreight and Branch Manger,

Optimising Airfreight

Mainfreight International notes there are many things to be determined: "You arrive at the airport as cargo much earlier than the passenger does and you are handled and mixed in with other commodities. There could be conflicts of interest, of course, in regard to temperature zones. So there are a lot of things that need to be considered as an international forwarder [when determining how] to position yourself as a piece of cargo and how would you like to be treated."

Getting prepared for being on the ramp

A problematic stage often encountered by pharmaceutical firms occurs after flight when cargo is transferred from the aircraft to the airline warehouse.

In preparation for this stage, some of the promised offerings from airports include cooled transfer trucks, reflective blankets and temperature controlled warehouses en route. However, Mark notes that he has encountered issues with these on one occasion or another: "…the worst being product left in a non-temperature controlled warehouse for over 36 hours despite being booked, and paid for on a temperature controlled service."

One solution for this situation is the use of active cooling device, - efficient but can be expensive and can need intervention – re-icing, mains plug power, fresh batteries, etc…

Passive systems can be a good option here, but bear in mind that due to the added bulk this option is likely to increase the weight being shipped and therefore the cost needed.

Closing Remarks

Airfreight is an exceptional tool when applied successfully. While optimising the use of airfreight it is paramount to pay attention to addressing potential pitfalls that may be encountered. This way your return on investment will be more safeguarded.

Want to learn more about optimizing your airfreight strategy?

The Temperature Controlled Logistics Europe Conference will analyse the process of optimising air freight in-depth and is set to give attendees key takeaways on the matter. Turnover for more...

ColdChainIQ
Temperature Control Logistics
& Quality Network

15TH ANNUAL COOL CHAIN
TEMPERATURE CONTROLLED LOGISTICS EUROPE

Don't let your Future be Frozen Out

Two prime profiles of what not to do in cold chain logistics recently were presented within two US criminal investigations.

May this year witnessed the **$33m case** featuring US firms SB Medical Inc. and TC Medical Group – both based in Toronto, Canada and St. Michael Barbados, plead guilty to their involvement in a multi-year medical conspiracy. (Indictment Case No. 1:14-cr-397).

In regards to the misdistribution practises regarding the pharmaceuticals in question, the FDA notice states:
"Instead of storing pharmaceuticals at cool temperatures as required for many of the pharmaceuticals, members of the conspiracy used unregistered commercial mailboxes, residential backyards and porches, basement rooms, garages, kitchen fridges and freezers, which did not have adequate lighting, ventilation, temperature, humidity, and security as required for the safe storage and handling of the prescription drugs and devices."

Also, back in 2013, a **guilty plea** was lodged by Gallant Pharma International Inc., headquartered in Arlington, Va., to two counts of importation fraud.

In the statements of facts filed with the plea agreements, Gallant Pharma admitted that the company sold "cold chain" drugs and shipped and received those drugs with ice packs that sometimes melted, and were not with dry ice used by legitimate drug distributors.

Of course cases of this extremity are rare, however most cold chain suppliers will have faced the occurrence of spoiled pharmaceuticals when quality control has slipped.

The Cost of Quality

Undoubtedly, the supply chain is complex to navigate with the maintenance of quality and security being of prime focus. New compliance requirements have translated into additional expenses for cold chain suppliers to account into their overheads, leaving many of these commercial firms searching for the most cost-efficient solutions.

Although, amidst the corporate pressure to heighten cost –efficiencies and financial savings in the cold chain, the industry must not let its focus on the gravity of compliance responsibilities waiver.

Cold Chain IQ has compiled a set of key considerations to contemplate should you be presented with the temptation to cut corners in quality in the name of costs.

Don't Just Take The Vendor's Word For It

According to the Centers for Disease Control and Prevention's (CDC) estimation, around $300 million worth of vaccines alone are lost annually due to improper storage and distribution.

Emilie DeGlise of Celgene International mentions that when it comes to data on effectiveness of transport packaging: "Don't be too confident in what the suppliers give you because it [does] not always represent the reality of a shipment."

" I have heard stories of alleged cold rooms being available in certain airports, but once you go on-site you find there is not even a thermometer installed.

- Eugenio Fillippi

"To give you an example, some ... test their blankets in a thermal chamber but it's not representative at all because in a thermal chamber you have temperatures but you don't have the sun shining, you don't have the humidity, so the real conditions are not [there].

"The real condition is that your shipment is changing temperature all the time, it could wait on the tarmac [for] two, three, four hours, could then be in a plane - a very cold temperature and etc…"

Choose Your Partners Wisely

On the matter of selecting which third party providers to work with, Eugenio Filippi, Pharmaceutical Logistics Senior Manager, notes that it pays to ensure they are trustworthy.

"I have heard stories of alleged cold rooms

Don't let your Future be Frozen Out

being available in certain airports, but once you go on-site you find there is not even a thermometer installed.

"If it is a new partner, a new lane, a new process, who should you trust with the data gathering? "If someone in a sub-tropical region of the world, for example, swears to you there are enough electrical outlets to recharge your box, do you take it at face value, ask for evidence, fly in to check it in person?

"Would you entrust the truck driver of your shipper, for instance, to perform the on-site inspection to determine the high and low risk elements of the route in question? Does the person have the understanding or know-how to perform such a task?...

"Once you have all the relevant data I do agree that doing a proper qualification should be rather straightforward, however, I have yet to see a simple "how to" guide to tackling the nitty-gritty of gathering such information in different countries, involving potentially dozens if not hundreds of partners.

"Ultimately, who do you trust?"

Don't Neglect The Drivers Of The Supply Chain

The Freight Transport Association notes that the logistics industry is suffering a driver shortage.

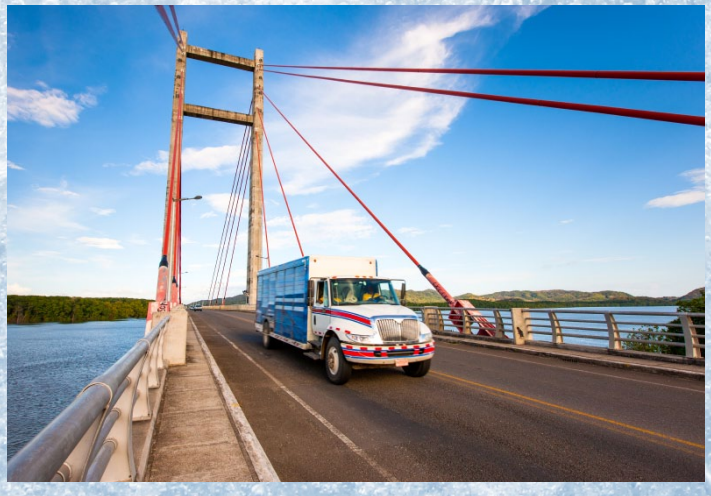
With the driver industry suffocating from an aging workforce and a lack of new entrants – down to licence acquisition, lack of understanding, poor sector image and low quality driver facilities.

Some predict that a plummeting supply of drivers could spark a rise in price point in the near future.

Don't Charge Ahead Without A Crisis Plan

In an unforeseen crisis, a contingency plan can facilitate extensive damage control. On this matter, World Courier notes: "It is important that all personnel take contingency planning seriously—even if the events which would trigger the plan seem remote and unlikely."

"Contingency planning is the process that prepares us individually, corporately and on a local and global level to respond coherently to an unplanned event. Being involved in logistics and supply chain, it's easy to focus on big international events with intercontinental travel or problems with the weather. But it's equally important to consider smaller and more local issues."



"What happens if norovirus spreads through the entire office staff? What happens if a supplier goes out of business?"

Don't Leave Your Data To Gather Dust

Data has ground-breaking potential for the healthcare industry. In a recent study by Capgemini, organizations reported an average 26% improvement in performance due to their use of big data analytics, with respondents expecting to see a full 41% improvement over the next three years.

In regards to utilising data analysis within cold chain, Emilie DeGlise of Celgene International notes that within the results some surprises may surface. "For example, we felt that shipments take only two days but at the end you see that, no, it's taken five days. But you can analyze very professionally where you [have] "lost" time and then you can begin to improve with your carriers or with your partners..."

Don't Allow Fraud To Burrow Its Way into Your Cold Chain

Remember a long supply chain only needs a single weakness for a breach to take effect. So investment in quality security systems is vital. Pfizer notes that recent years have seen a significant rise in the level of counterfeit medicines reaching consumers across Europe through illicit sources such as the internet as patients scout the web to find cheaper offers with an element of convenience.

The EU's Falsified Medicines Directive looks to safeguard the integrity of pharmaceutical supply chain from the presence of falsified medicines. Implemented in 2011, this directive influenced the cold chain with added control obligations in regards to starting materials and inspections of active substance producers and excipients in medicines.

View Cold Chain IQ's Cold Chain Compliance Milestones **here.**

Regulation Penalties Are Costly

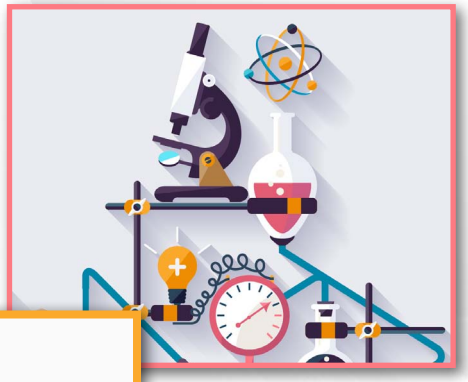
The consequences of mishandling pharmaceuticals not only translate into substantial health risks for consumers and detriment to consumer trust should the news hit the public domain in a big way, but also in the form of penalties. E.G License suspension, refusal, restrictions from importing and sale in Europe. In response to those tempted to risk compliance levels slightly to keep costs down, Nigel Wing of Global Head Life Sciences & Healthcare, DHL Global Forwarding notes: "Amongst other aspects, we are talking about patient safety, product efficacy, high values & company brand reputation. For a responsible company this type of risk is not acceptable or sustainable long term."

To conclude, although your bottom line may endure slightly more stress due to added GDP requirements, it certainly pays to ensure your priorities do not become distracted by the presence of attractive costs.

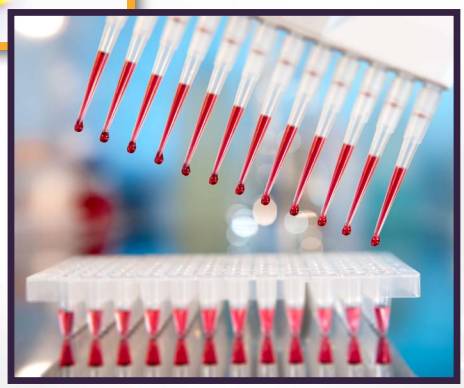
It's Never Too Late to Document Your Validation Approach

Gary Hutchinson, President of Modality Solutions

d Documentation strategy for your cold chain management validation practices has evolved over the last several years. The FDA and other regulatory agencies are requesting more and more specific information in the filing to confirm the impact to drug product during transport, and the effect transportation hazards have on shelf life. An overall strategy of providing minimal documentation in the Biologic License Application (BLA) has evolved to provide a more complete and comprehensive review of the stability data, verification studies, packaging qualification and process validation activities in the BLA to support questions in the pre-approval inspection (PAI). The outdated "don't ask, don't tell" approach has given way to provide cold chain qualification and validation data that is reviewable by regulators and is expected to be discussed in the PAI process. More and more, data that has not been submitted and reviewed in the BLA is more difficult to use as justification for temperature ranges set outside of labelled storage conditions or justification for drug product release after excursions in distribution outside of labelled storage conditions.



Documentation for sections 3.2.P.3.5 Process Validation as it pertains to distribution and cold chain activities should include the following elements:



Packaging Qualification

- Primary packaging – container closure integrity, sterile barrier, physical integrity, and leachables and extractables after agitation
- Secondary packaging – physical integrity and label legibility
- Thermal packaging – physical integrity and thermal control (after physical integrity testing)

Process Validation

- Performance qualification in qualified packaging in representative transport lanes

Documentation strategy for your cold chain management validation practices has evolved over the last several years. The FDA and other regulatory agencies are requesting more and more specific information in the filing to confirm the impact to drug product during transport, and the effect transportation hazards have on shelf life. An overall strategy of providing minimal documentation in the Biologic License Application (BLA) has evolved to provide a more complete and comprehensive review of the stability data, verification studies, packaging qualification and process validation activities in the BLA to support questions in the pre-approval inspection (PAI). The outdated "don't ask, don't tell" approach has given way to provide cold chain qualification and validation data that is reviewable by regulators and is expected to be discussed in the PAI process. More and more, data that has not been submitted and reviewed in the BLA is more difficult to use as justification for temperature ranges set outside of labelled storage conditions or justification for drug product release after excursions in distribution outside of labelled storage conditions.

Documentation for sections 3.2.P.3.5 Process Validation as it pertains to distribution and cold chain activities should include the following elements:

What to expect from Pharma Logistics IQ

- Drug product physical stability studies with release testing

Documentation for sections 3.2.P.8.3 Stability Data as it pertains to distribution and cold chain activities should include the following elements:

• Long-term stability studies per ICH Q1A Stability Testing of New Drug Substances and Products for confirmation of shelf life

• Accelerated stability studies per ICH Q1A Stability Testing of New Drug Substances and Products for justification of effects of temperature exposure outside recommended storage conditions

•Additional temperature-stress studies to evaluate the effect of short-term excursions of temperature outside recommended label conditions per ICH Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological / Biological Products

The BLA submission is the opportunity to show the qualification and validation data and support stability studies. The PAI inspection process is the opportunity to show process controls. The focus at the PAI is to review the validation master plan documentation to show the proper process controls are in place to confirm the product quality limits demonstrated in the BLA are achievable. The focus in the PAI should be in two key areas:

Standard Operating Procedures

- Product put-away and storage
- Inventory control
- Drug product picking
- Pack-out instructions for thermal packaging

Nonconformance Management

- Monitoring and controls
- Allowable exposure limits outside of labelled storage conditions with supporting stability studies
- Material traceability / inventory control processes

A medicinal product can take a variety of paths from the manufacturer to the patient. In some instances, a drug product can route directly to the patient. In others, there are a series of lanes in the distribution chain where the drug product may be subject to variable environments. Principles of process validation (including design, operational and performance qualifications) can be applied with good distribution practices (GDPs) to confirm portions of the supply chain are validated (excluding unforeseen transport events and the impact of extreme weather conditions).

An Implementation Strategy is Key

Your implementation strategy for preparing for BLA submission and the subsequent PAI should be well- defined and understood by all key stakeholders in the cold chain as quickly as possible. Your approach should be documented in a validation master plan. Some keys to success to consider are:

Network Design and Partner Selection:

1. Confirm expected channels of distribution as soon as possible
2. Select channel partners and physical location(s)

What to expect from Pharma Logistics IQ

for each channel of distribution
3. Conduct site assessment and quality management systems review
4. Prepare assessment report and track improvement against recommendations
5. Execute quality agreement as part of commercial terms
6. Implement management review metrics as part of management review process

Packaging Qualification:

1. Clearly define your temperature profiles and your justification for use
2. Perform operational qualification (OQ) study designed to expose the drug product to an approved composite (or representative) simulation of the distribution environment
3. Confirm or conduct operational and performance qualification (PQ) on the shipping systems as required (active vs. passive) after vendor data evaluation
4. Design monitoring and controls strategy based on qualification data

Process Validation and Shipping Studies:

1. Create validation master plan for drug product validation activities
2. Examine the interaction of each primary container type with the product for possible interactions.
3. Generate physical stability at the earliest possible opportunity in development with bulk secondary packaging
4. Apply to all subsequent secondary packaging since hazard exposure will exceed any within the commercial supply chain

A validation master plan for distribution along with specific product annexes can align the disparate activities already completed into a comprehensive and cohesive approach to distribution process validation.

The validation master plan gives an opportunity to discuss risks and mitigation strategies, qualification approach, validation approach, and monitors and controls. Sections can include discussion on warehousing and storage, product transportation, shipping configurations, methods of temperature control, and packaging.

Shipping studies must include both physical packaging integrity and drug product quality. Any proposed shipping qualification plan that does not include any testing of drug quality post shipping compared to specifications and/or control samples will be challenged. The regulatory agencies are expecting to see some post-shipment drug product studies to confirm quality after transport.

Protocols for shipping studies should be split into operational qualification (OQ) and performance qualification (PQ) - each type of protocol achieves difference results. The OQ protocols show in controlled laboratory conditions that the control in the proposed design space is achievable. The PQ protocols show in field conditions the process is robust and repeatable.


Pharma Logistics IQ
Supply Chain

Blowing Cold

By Alan Kennedy

It's a lips may pay service but much of the pharma-logistics sector remains dormant when it comes to genuine supply chain integration

Ask any stakeholder in the pharma supply chain whether collaborative working is a good thing and you'll nearly always get an unequivocal 'Yes'. It is fair to say that most pharma supply chain stakeholders agree that there is a wealth of benefits associated with collaborative working. But in practice real examples of integrated working in pharma-logistics remain few and far between.

Why is this? Is it because big monolithic companies don't have the flexibility or motivation to challenge habitual inertia? Is it because of entrenched attitudes, silo mentalities and departmental protectionism? Or is it simply because man's basic commercial instincts favour discord over concord?

Wholesale Change

In fact, it's all of these, and more. Objective reasoning can be one of the first casualties when it comes to existential questions around uncertainty, change and personal survival. Rationalising the status quo, however imperfect, is always a lot easier than justifying wholesale change.

'Why would we want to put all our eggs in one supply chain basket?', it can be argued. 'What about if we get in to bed with a bad partner?' And 'Who pays if we get let down? And so on.

These, and other censorious questions, are often enough to paralyse even the most earnest of integration missions. And, sadly, such mentalities reflect the inability of many hidebound commissioning parties to abstain from the time-worn, yet ultimately futile, tradition of nailing fellow stakeholders to the floor in their relentless attempts to squeeze out ever-lower prices.

Faint-hearted

The reality is that without across-the-board management support, without the right partners and without 100% commitment, a sustainable integration strategy can never be made to work. Today's relentless pace of change, remorseless competition, entrenched perceptions, vested interests and feelings of insecurity can all converge to make it difficult for companies to make the comprehensive internal and external relational changes necessary. Genuine supply chain integration is not for the faint-hearted.

The enormous challenges of pursuing integration must never be underestimated. Nonetheless, withthe fundamentals in place, all the perceived and real barriers to integration are surmountable. By planning ahead, selecting the right partners and getting the correct controls in place, the benefits of collaboration can be secured while keeping all the attendant risks within acceptable limits. 'Real' integration is emphatically possible - but only when the entire supply network is involved from the outset and works smoothly and seamlessly towards common goals.

Asymmetrical Integration

The supply chain oppression and subordination that plagues some other industries is alive and kicking in the pharma-logistics sector. It is a fact that the majority of so-called 'collaborative' arrangements between shippers and their 'Tier One' partners then go on to omit, marginalise or railroad the numerous, upstream suppliers, service providers and other stakeholders that go to make up a supply chain. It is integration at its asymmetrical worst. It's symptomatic of an archaic 'buyer as king' mentality; one that is wholly dependent on a traditional 'master-servant' hierarchy of control, function and communication.

In a properly integrated supply model, every member not only needs to be valued, but needs to be convinced that it is in their individual interest, as well as in the network's collective interest,for

Blowing Cold

By Alan Kennedy

them to actively contribute. Each network member must be appreciative of the symbiotic nature of the relationships involved and have respect for the contribution of others.

And crucially, logistics providers, product suppliers and all other supply chain stakeholders must have 100% confidence that their fingers are not going to be jabbed out of the collaborative pie when it comes to the sharing out of bottom-line benefits.

The Bottom Line

It's not that supply chain integration doesn't work. It does. It's just that it is not easy to make it work. Many collaborative partnerships fail at the first hurdles. But, although there is a common perception that the 'buyer always has the most to gain', an integrated supply network that is conceived rationally and executed properly, will invariably work to the benefit of all parties.

Drugs Via Drone Delivery

Contributor: Cathy Roberson

Drones are constantly in the news with the likes of Amazon, Wal-Mart, Facebook, Google and more testing them as delivery options. Imagine receiving a book you ordered via Amazon's drone delivery service or perhaps a hard to find part for your classic car by way of Facebook's drone delivery service. Depending on one's location and need as well as lobbying efforts such as Amazon's rumored spend to educate US government officials on a range of topics including this mode of travel; the future for drone deliveries is a reality.

For healthcare professionals, the use of drones has huge benefits in particular the ability to reach remote areas that lack proper infrastructure to deliver lifesaving drugs and other necessities. Many tests are underway to determine its viability but as one can imagine, it is under much government scrutiny and regulators in many countries are working with the industry to develop requirements for the delivery and flying of drones.

Last year's devastating earthquake in Nepal saw drones in action. Global Medic, a Canadian charity that provides disaster response in the form of medical assistance, flew drones over the affected areas to study and 3D map the worst hit zones. The information was then passed to rescue workers on the ground to show them exactly where to go.

In Africa, medical deliveries by drone are already underway. US-based startup Matternet has partnered with the government of Malawi and with UNICEF to deliver infant H.I.V. tests within the country and in Rwanda, another start-up, Zipline, is delivering blood and pharmaceuticals to remote locations in hours rather than weeks or months. According to Zipline, its system's speed makes it possible to maintain a "cold chain" and when it reaches hospitals, they will not land but will drop small packages from very low altitudes. The supplies will fall suspended by simple paper parachutes. The drones will then return to a home base, where they will be prepared for a new mission by swapping in a new battery and snapping in a new flight plan stored in a SIM card.

What to expect from Pharma Logistics IQ

Drone deliveries are not only in emerging markets. Within the US, NASA partnered with drone startup business, Flirtey to deliver medicines and other medical supplies to an annual free clinic in Virginia. The entire operation took about two hours as Flirtey separated the medical supplies into 24 small packages which were then transported by the drone. The pharmaceuticals were lowered to the ground via tether and health care professionals at the scene received them.

In Europe, DHL is utilizing drones to deliver drugs and other urgent supplies to a remote island in the North Sea. The island, Juist, is only accessible by a once daily ferry service and regular passenger flights. According to a press statement from a DHL Parcel spokesperson back in 2014, deliveries are secured and all types of drugs can be carried except those which are dependent on refrigeration, as a refrigeration unit may be too weighty for the 'parcelcopter' to carry.

Also in Europe, a very interesting product has recently been introduced by Flash, a logistics provider that focuses on premium freight delivery services. Flash's drone is one of the more unique in the market. Each drone is equipped with biologistic isothermal packaging for temperature control and monitoring and travels on a predefined and programmed flight path directed by longitude and latitude coordinates. Testing is expected to take place this year at the University Hospital Center of Bordeaux, a partner of Drones for Life which is a group of healthcare, technology and development experts trained to route and test drones safely and one in which Flash is a member. The delivery service itself will be marketable in Europe by 2017.

Is drone delivery viable? According to various market research companies, the estimated market size of the commercial drone market was about $609 million in 2014 and is expected to grow roughly to $4.8 to $6.4 billion by 2021. The market faces numerous challenges, most importantly how to share air space with larger airplanes as well as privacy and security concerns. However, its benefits in delivering life-saving pharmaceuticals to remote areas cannot be denied and perhaps this is 'secret sauce' within supply chains. But, like many other great innovations, its use will evolve and expand over time to perhaps delivering to the elderly and shut-ins to delivery within 'smart cities'. The possibilities are endless.


Pharma Logistics IQ
Supply Chain Security

Pharma iQ
a division of IQPC

The Hospital Perspective:

Lessons on UDI Implementation

at the Point of Care

UDIs & Traceability for Medical Devices 2016

The Hospital Perspective: Lessons on UDI Implementation at the Point of Care

The objective of UDI regulation to trace medical devices throughout distribution and use is undoubtedly beneficial for industry transparency and standardisation. The ability to scan and identify at the point of use preserves patient safety in that it develops communication via data sharing, making adverse events easier to recall and address.

The electronic capabilities of UDIs are also directly advantageous to manufacturers themselves. With Dawn Fowler, Senior Manager, Labeling & Documentation Endologix, noting that the identifiers have enabled the firm to streamline business practices, reduce turnaround times and eliminate time consuming and costly manual processes. Barcode technology chains can provide a good return on investment for companies with large amounts of SKUs by automating the process and avoiding manual pick/packs. The manufacturers can then manage electronic movement throughout the process as the 3PL or distributor inventory pick. The distributor can then transport goods much more efficiently to hospitals, customers. (1)

In addition to this, the reduced supply chain costs can filter down to shrink costs for end users and patients.

However, the task of realizing these advantages by deploying UDIs for medical devices stands as a vast project, with the practical challenges of efficient and compliant implementation looming large.

Some of the implementation roadblocks that confront and hinder today's hospitals include:
-Bar codes not being well printed
-Unreliable bar codes
-Superfluous labels on a device, mostly intended for the manufacturer's use that drown out the label of interest for the hospital.

With a view to contribute to the industry's ongoing progression, Pharma IQ collates the lessons learnt by hospitals during the implementation of UDIs for medical devices and how the conduct of manufacturers and hospitals could be altered to not just optimize this

project's roll out but to avoid incurring any detriment.

With the initiation of this project, both external and internal communication is crucial for manufacturers, especially when dealing with multiple global sites. Employees must fully appreciate the importance of the UDI project as varied departments need to be coordinated for the sequencing of the implementation. This project impacts a range of departments as UDI implementation is both technical - print technology and IT infrastructure, as well as people related – finalizing data governance organisation, making art work design decisions, evaluating partners of the supply chain. Inge Ørnhøj from medical device manufacturer Coloplast A/S noted, this "… is a major challenge and means that we have to work closely together with people that normally do not talk the same language basically." (2)

Master Data

Inconsistencies caused by varied bespoke numbering systems on product databases have led to complications with UDIs. For instance, in the report Strength in unity: The promise of global standards in healthcare McKinsey stated that: "The US Department of Defense discovered that hospital product catalogues had problems matching the correct manufacturer identifier for 30% of the medical devices they listed in their catalogue; at a leading US GPO, a single part number in the product catalogue linked to 9 identifiers and different products from different distributors."

The research paper added that extensive effort is required to keep catalogues current with the correct detailing's. Although, "Despite these efforts, inaccuracies are prevalent, leading to erroneous transactions and the need for costly reverse logistics and canceled procedures because the right products are not available." (6)

The lack of quality with master data plants numerous road blocks for the University Medical Centre Schleswig-Hostein in Kiel and Lübeck, Germany. There PD

The Hospital Perspective: Lessons on UDI Implementation at the Point of Care

Dr. med. Hajo Reissßmann, MBA and Michaela Berlich together with a number of colleagues run a project to document device usage at the point of care. They knew that the task of tracking which materials and devices are used in the care of specific patients relies on accurate master data. Dr. Reissmann explains that in some instances "….we're [enduring] very painful experiences, [revealing] that availability of high quality master data and product labelling is sub-optimal to say the least. And so there's a very specific driver for us to try to improve how industry collects their master data, communicates their master data and labels their products."

Hospitals can encounter major difficulties in even obtaining the relevant master data. This is often experienced while manufacturers are in the process of transferring systems.

In one case with a manufacturer switching to the GS1 system, the GTINs for their products were communicated to the hospital of focus, however the actual products being delivered displayed HIBCs which had not been communicated to the hospital.

The hospital then encountered issues in actually obtaining the HIBCs from the manufacturer, constantly receiving responses that the HIBCs were irrelevant due to them being 'phased out' and so were unneeded. The complication had to be escalated to being communicated to the CEO of the manufacturer and where it was finally understood that this information did in fact need to be transferred.

In regards to how hospitals should adapt their responses to the implementation of UDIS a dominant factor was not to underestimate the level of resources needed for master data acquisition.

Dr Reissmann notes that manufacturers should consider joining a master data pool so that they only need to supply their master data to one partner in one well defined format, and all customers can access them through a unified

The Hospital Perspective: Lessons on UDI Implementation at the Point of Care

mechanism. "The traditional many to many communication on master data is extremely laborious and error prone. So we have a very strong opinion that exchanging master data through pools, through a hub, is very advantageous." He added that manufacturers already have to populate a master data pool (the NPC = National Product Catalogue) to qualify for trade with Australian hospitals, and that the British NHS is implementing a similar system.

Physical Display

On the subject of the physical presentation of UDIs on devices, some have noted the need to preserve the prominence of the unique identifier amidst numerous manufacturer-specific identifier codes. Otherwise in a clinical context, the UDI isn't clear to the professionals handling the device and so it is vague in where the scanner should be directed.

Some hospitals have adopted unique approaches towards UDI implementation. One hospital decided that if a device lacked an unmistakeable identifier on its label, they would re-label the device in-house to avoid confusion at the OR. Approximately 50% of the devices were re-labelled amidst the initial stages of this project to aid productivity. Realist considerations must be made if these bespoke approaches are going to be used. For instance, whether the hospital holds an adequate workforce to perform this comfortably. Also, a specialist has noted that in the case of a product mix up the entity which labelled the product last is deemed to be legally responsible for the confusion.

Leveraging Buying Power

Instead of acting as individual entities, hospitals are called to compound their purchasing power to invoke change. Dr Reissmann stressed that the lobbying of collective buying power is necessary: "….in order to make clear to manufacturers and vendors that unique device identification and master data communication must [be of] quality [and] are of importance. So [hospitals] should join forces on that, and not try to do it individually, because approaching

manufacturers as an individual hospital or as a small GPO doesn't work. It won't move the manufacturers to do anything."

In conclusion, on the route to realising the benefits of UDIs for medical devices and meeting the regulatory expectation, the conduct of both manufacturers and end users could be altered.
These methods nclude:

Hospitals

- Don't underestimate the level of resources needed for master data acquisition.
- Instead of acting as individual entities, hospitals are called to compound their purchasing power to invoke change.
- Consider adopting unique approaches towards UDI implementation – consider all of the pros and cons

Device manufacturers:

- Preserve the prominence of the unique identifier amidst numerous manufacturer-specific identifier codes
- Be alert to the extensive effort is required to keep catalogues current with the correct detailing's in response to bespoke databases.
- Consider entering a master data pool

These amendments in industry conduct could go a long way to enhance the success of the practical implementation of UDIs for medical devices and evade any threats to patient safety or waste in resources.

Dr. Hajo Reißmann, will be present at this year's UDIs and Tracebility for Medical Devices conference to provide further industry insight.

SERIALISATION & TRACK AND TRACE DEADLINES: PRINTABLE WORLDMAP

As the serialisation industry prepares for various approaching deadlines all over the globe, Pharma IQ has created a printable map to assist with your worldwide track and trace compliance strategies.

EU

FMD Delegate Act live imposing **Feb 2019 deadline.**

Pharmaceutical Serialisation & Traceability 2016

SPEAKERS:

Dhermita Desai, Operations Projects Team Manager, **Concordia UK**

Michael Kinsella, Industrial Operations Deputy Director, **Servier France**

Stefano Zanobini, Serialization Global Project Manager, **UCB Italy**

Daniela Guttmann, Packaging & Serialisation Product & Service Manager, **Vetter - Germany**

UKRAINE

Feb 2017 - Serialisation Sales Implementation Phase 1 due for Manufacturers and wholesale distributors.

Track and trace postponed

Aggregations requirements likely (4)

RUSSIA

Draft of regulation has been under consultation and is due to be laid down by June 2016

Nov 2016 – Pilot programs should begin

Jan 2017 – 1st drug class serialisted - The seven high-spending disease classes such as treatment of haemophilia or multiple sclerosis and patients after organ transplantation.

Jan 2018 – 2nd drug class serialisted Vital and essential medicines. Subject to upper price limit set by the authorities.

Jan 2019 – 3rd Drug class serialised all other medicines (5)

CANADA

Technical barcode committee – bar coding project

December 2017 – phase 4.

JAPAN

Draft serialisation legislation reached the end of public review in June.

According to Be4ward Non-biologics serialisation deadline proposed for **2021.** (1)

KOREA

Jan 2016 - All pharmaceutical products need to be serialised. (3)

USA

November 2017 - USA Drug Supply Chain Security Act (DSCSA) 4 years post enactment, drugs must be serialised by manufacturers at the saleable unit and case level.

Pharmaceutical Serialisation & Traceability 2016

SPEAKER:

Ravi Kalyanaraman, Associate Director, **Bristol Myers Squibb - USA**

SAUDI ARABIA

Clarification on deadlines pending.

PAKISTAN

The release of new requirements is expected soon, date is unknown.

PHILIPPINES

Serialisation regulations in draft, timelines are expected to be short.

BRAZIL

At the time of writing - serialisation law RDC54 still stands. A new draft law, which would invalidate the existing legislation, has received Senate approval and is pending public consultation from ANVISA – publish date is scheduled for September.

Proposed timelines: Pilot for 3 batches in 1 year, 1 year's consideration and establishment of final requirements, followed by 3 years to enforcement. (1)

LIBYA

Jan 2017 – Expected deadline for unit level serialisation

Draft regulations pending.

ETHIOPIA

Understood to be discussing serialisation and conducting summer workshops. (1)

INDIA

Looking to formulate an industry / ministry working group to combat complications encountered (1).

TAIWAN

Jan 2018 – stated deadline - All prescription drugs medication barcode requirements and implementation timelines (4)

EGYPT

Serialisation implementation plan signed by the MoH is rumoured to be launched soon. (1)

CHINA

Potential amends to drug tracing system requirements is in progress, after a notice was issued by the CFDA. Concerns have been communicated to the new proposals which also cover medical devices. (1)

MEXICO

Jan 2018 – Operational database enactment for Draft Mexico Regulation Amendment for general law of health. (4)

NIGERIA

Global standards in regards to serialization are being shaped, no date of release known. (1)

JORDAN

1st July 2018 – AI 2d with GTIN, Lot number and Expiry date required.

1st July 2020 – Serial number added. (1)

6th Annual
Pharmaceutical Serialisation & Traceability

Serialisation Strategies

Top Tech Integration Considerations

Pharma iQ
a division of IQPC

Serialisation Strategies

Top Tech
Integration Considerations

Roger Bate from the American Enterprise Institute estimates that global economy is hit by $10 billion in losses due to counterfeit and substandard medicines alone. Life loss, he estimates, equates to around 100,000 deaths a year – primarily felt by emerging markets.

These costs are part of what sparked the introduction of serialisation – the method of tracing the lifecycle of the medicine via a serial number.

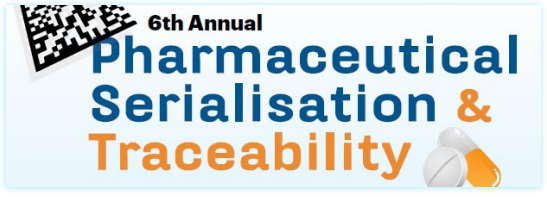
Undoubtedly, technology stands as a keystone in a controlled track and trace system.

Therefore, it's imperative for pharma and biotech firms to invest time and money in the right technology, the right partners and then focus on the integration and harmonisation of the serialisation process from a departmental and technological perspective. This integration is required across warehouse systems, shipping systems and packaging systems on an international basis – with some country specific regulations still pending.

Also, the invasive and complex nature of facilitating high-speed, mass data handling produces multiple technical considerations.

In light of these points, Pharma IQ has compiled a set of key technological factors in regards to the integration and harmonisation stages of a serialisation strategy.

NOTE: Opinions expressed in this piece are the respondent's own and not that of their company.



Serialisation Strategies
Top Tech
Integration Considerations

Connectivity & Control

When it comes to technology, integrated connectivity is vital for traceability and allowing data to flow to various departments.

In regards to this matter, Michael Kinsella, Industrial Operations Deputy Director, Servier notes: "We're looking for solutions that are connectable, IT solutions that are connectable, but ones that don't impose pre-defined connections to other IT systems.

"The idea of connectivity is very important and this gives you the ability to have a modular approach. You should have a system which is scalable."

Pharmaceutical companies and CMOs require machines with modular capabilities throughout the entire serialisation process in order to cater for legislation and cost profiles.

According to an **Industry Week article** by Joe Whyte of Rockwell Automation: "Printers, vision-inspection camera systems, handhelds and RFID equipment should be able to integrate with the control system for all serialisation line-level components from one cabinet. This add-on capability helps ensure minimal interruption of the production process and simplified validation. Integration of high-speed coding and verification capabilities also should meet industry standards, including EPCIS."

To aid firm wide data communication, Joe Whyte notes that the control system of a serialisation machine should feature a programmable automation controller through dedicated Ethernet control network architecture.

He adds: "The system should provide for the generation, randomisation, aggregation, synchronisation and management of serial numbers on all product-packaging levels. It should be in accordance with EPC Information Services (EPCIS) standards and support the transaction of serialisation data to third-party systems, such as SAP, IBM and contractor systems."

Functionality Flexibility

For CMO's in particular flexibility is required in order to facilitate the requests of pharma and biotech companies.

So the needs of customers will have to be taken into account with technological considerations, like secure segmentation abilities within the process of data flowing or sample message activities in the production process- whether to include as a destroyed message.
Alexander Ulbrich - Information Technology Manager of Vetter Pharma-Fertigung GmbH & Co. KG said that customer interface adaptability was a hurdle the firm had to overcome.

He said: "So for us the biggest challenge for

integration was for us to build customer interfaces because we have a couple of big customers and all of these customers have their own standard interfaces. There's not a global standard, so each of the customers has their own standard interface and it means for us, as the CMO, we have to adapt to this standard of the customer.

"So we have already a couple of different customer interfaces which all communicate at the same functionality, for example commissioning or destroying reports, but on a different way, in a different format."

Harmonisation

Technological harmonisation requires cognitive and financial investment in the choice of hardware and software and then a methodical roll-out across units.

Although, pre-existing solutions may have to be incorporated in this integration. Localisation factors may have to be considered because of language, the IT architecture, the geography or the physical structure of the factory. However, experts note it is vital that there is a central management group that can support all sites, respond to maintenance tickets and maintain maximum levels of harmonisation to allow for solidarity as well as experience sharing between units.

Michael Kinsella states: "This is real change, in the industry in general. Most factories would tender for business and manage their business as marketing authorisation holders. This is really, now, a new day-to-day governance system."

Some firms chose to utilise the same printing and verification machines across its packaging lines. As the factories operate via the same software and printing machine, theoretically, individual units should hold the same philosophy for aggregation.

Automation

Within the process of harmonisation there could be opportunities in the serialisation project to reduce or to automate some quality control activities for operators.

Michael Kinsella notes: "Simply take one example, if we print on every box and we verify the print is correct then we can eliminate the human check for the print which could reduce the risk of a human error because 100% of the boxes will be checked automatically.

"It's one example but you could have other harmonisations of processes or quality checks. Checking the number of boxes in an outer, for example, it will happen automatically if we have aggregation."

Global Data Exchanges

Pharma firms have to consider country specific serialisation requirements. This is complicated by the fact that a selection of these requirements are currently in draft stages, blocking the prospect of attaining a completely future proof solution.

Industry experts stress that it's important for pharma and biotech firms to work towards one global standard and not to restrict themselves to the capabilities of individual software providers.

Michael Kinsella states: "As the amount of countries increases, we see, in our view, that you would have a centralised service for all of the data reporting to the markets and this centralised service then could also work both ways. You could receive numbers coming from outside when we act as a CMO for other companies, and it would also send numbers outside from the factories, where we generate the numbers internally."

"So, the key challenges or the key steps in the project are really to put in place the foundations to be able to print, verify, to generate the reports before the product leaves the factory and then to be also able manage globally all of the data exchanges required."

Considerations on an international front also include the location and specification of the global repository to store data and the site manager to capture data which will be transferred to relevant regulators.

In regards to these considerations, Alexander Ulbrich recalls that for each region one server system would be used: "So for... the site server and line controller system, we decided on the ones that we [would] use, so at least one site server per region ... one for Europe, one for Asia and then one for America."

Alexander's firm then opted to use the same provider for the line controller and the site server to prevent difficulties with the interface between the two.

Added tips will be discussed at this year's pharmaceutical and traceability conference.

Pharma Logistics IQ

Regulations

What to expect from Pharma Logistics IQ

GDP Compliance Update - Q2 2016

In regards to the ever evolving landscape of good distribution practises, Cold Chain IQ has compiled a rundown of the latest updates seen across the globe over the last few months.

New Russian GDP Guidelines Activate

Guidelines on Good Storage and Transportation Practice of Medicinal Products for Medical use from the Russian Ministry of Health came into effect on the 1st of January 2016. "The Russian GDP guidelines are based on EU GDP guidelines. However, the required infrastructure, monitoring, and commitment to modern quality system approaches in the Russian distributor markets will make implementation and compliance a challenge. Manufacturers should plan extra care in selecting and auditing their partners and should be prepared to provide significant support to ensure compliance if the final directives mirror the current EU compliance approach." – Gary Hutchinson of Modality Solutions.

GMP GDP Annex 16 – Coming into effect at 15 April 2016 certification by QP published – in progress.

The changes are mainly found in the 1st section of the document, looks at 3rd parties used in the process as well as importing stock for export holding a WDA(h). "The key to compliance will continue to be well maintained and documented internal quality systems rather than a third-party certificate of compliance. Common sense and practical approaches to ensuring drug quality in transport will continue to the gold standard." – Gary Hutchinson

Falsified Medicines Directive

This month saw a major movement in regards to the Falsified Medicines Directive, after the commission published the delegated regulation in the official journal outlining the details of the required safety features in the mission to conserve the medicinal supply chain of breaches leading to counterfeit drugs. This includes the specifications of the two dimensional barcode and the verification of safety features which include the integrity of the anti tampering device. This regulation is due to come into force from February 9th 2019.

German Associations Publish Paper On Temperature Excursions

Associations connected to the manufacturers of medicinal products collaborated to publish a paper that was forwarded directly to EU authorities in regards to the regulations. The document outlined new suggestions for apt techniques in assessing temperature deviations amidst transport of medical products. A response from relevant authorities is still pending. Gary Hutchinson said: "The addition of a set exposure period of 12 hours rather than the manufacturer's understanding of allowable exposures using their regulator-reviewed product stability data is fundamental flaw in this proposal."

Pharma Quality Update:

Quality by Design

Pharma iQ
Quality Training Series

Pharma Quality Update

Ahead of the Pharma IQ Quality Training Series in June, we speak to our expert for Quality by Design to find out the latest updates and forecasts for the industry.

Quality By Design Update

Richard Francis
Owner
Francis Biopharma

Pharma iQ
Quality Training Series

Quality By Design Update

Richard Francis, Owner, Francis Biopharma

1.What is the biggest QbD challenge for pharma companies?

Understanding the value proposition: the key is that following the systematic approach within QbD or an enhanced pharmaceutical development approach (as defined in the ICH Q8 and 11 guidances) the company will develop a more robust understanding of both process and product. Such an understanding is critical for maintaining product quality and supply of the product to patients.

This is the true value of a QbD approach and, still, many companies are yet to understand this benefit as they view it as a regulatory agency driven program and not the foundation too their own quality management system it really is.

2.How can this be addressed?

Though education, proven examples and communication from the regulatory agencies - which is coming in the shape of new guidance (ICH Q12).

3.If this hurdle in the market isn't solved what are the potential consequences for both the company at hand and industry?

Continuing drug shortages, increased risk to patient safety, increased regulatory agency enforcement and a general decline in the pharma industry.

4.Any case studies of QbD mistakes you have seen in your experience ?

The joint FDA /EMA QbD submission program and the lessons learnt from the Roche Pejeta QbD submission and the expectation of design space definition are both very useful.

5. Have there been any changes to QbD regulations or guidelines recently**?**

There is a new guidance ICH Q12 that will of course be useful to address many issues. Additionally, the FDA guidance relating to defining Established Process Conditions in relation to an overall process control strategy is also of significant use.

6. Are there any regulations or guidelines which may be changing over the next 24 – 48 months?

Yes, to ICH Q12. The official ICH statement concerning ICHQ12 is;

This guideline is intended to work with ICH Q8 to Q11 Guidelines and will provide a framework to facilitate the management of post-approval Chemistry, Manufacturing and Controls (CMC) changes in a more predictable and efficient manner across the product lifecycle.

There is currently a lack of a harmonised approach on technical and regulatory considerations for lifecycle management. While the concepts in ICH Q8, Q9, Q10 and Q11 provide opportunities for a more science and risk-based approach for assessing changes across the lifecycle, several gaps exist which limit full realisation of intended benefits.

The envisioned post-approval 'operational flexibility' has not been achieved. The main emphasis at ICH to date has focused on early stages of the product lifecycle (i.e., development through launch).

7. Why is continuous improvement important for professionals affected by QbD regulations? – What would you say to someone who thought it was a waste to invest in continuous improvement?

The issue with the guidances is they cannot specifically define all of the requirements associated with your specific needs. So the more you develop your understanding of the guidance's and also examine how others in your

industry interpret and use them, then the greater your capability will be to direct and manage the regulatory expectations. Without that capability the reverse will be true, hence the importance of knowledge in this ever developing and changing area.

Pharma iQ

Quality Training Series

What's on the horizon for GMP: A Compliance Update

When examining the known future for GMP compliance, there are a range of changes that the industry needs to brace for, including a new EU delegated act focused on investigational medicinal products. Here Pharma IQ outlines the GMP updates the market will soon be facing.

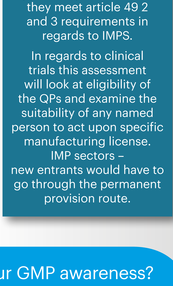
Future Annex 21 EU GMP Guide – Brand new for the importation of medicinal products, with an awareness of increased complexity of the supply chain network. Area of focus is concerned with the application of GMP on importation not just traditional GMP requirements at manufacturing sites. Updated draft for discussion at IWG February meeting in 2016.

New Delegated Act impacting GMP for Investigational Medicinal Products for Human Use – published in 2014, these regulations have been in limbo as the European portal for clinical trial applications needed to be in place before this regulation could be initiated. There are likely to be GMP implications from these clinical trial regulations and delegated acts. Consultations ended in Nov 2015. The results of consultation were released in Q1 of 2016.

The activation of new Clinical Trial regulations will require a new guideline for GMP Annex 13 in regards to GMP for IMP. Main changes are said to refer to labelling requirements – for immediate and outer packaging particulars – less flexible than existing requirements with no possibility of opting out. References are also made in regards to the cooperation between manufacturers and sponsors but some specific responsibilities have been removed under shipping requirements.

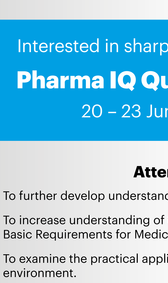
Future Annex 17 of EU GMP Guide Parametric Release - Re-titled as "real time release testing", consultation was launched in Sept 2015.

A revised version of this annex is being constructed with consultation finishing at the end of 2015. The first draft has noted that the scope is due to encompass the real time release testing approach in manufacturing.



Annex 1 of EU GMP Guide - Significant updates, in regards to the manufacturing of sterile medicines.

The outcomes of the consultation paper are predicted to produce adjustments to the landscape and further clarity on segments traditionally perceived as vague.



New GMP EU Guideline for Advanced Therapy Medicinal Products: Initially addressed by a revision of Annex 2 by specific ATMPs adaptation, however a new standalone document on GMPS for ATMPS has been proposed by the commission. This will cover commercial and clinical ATMPS and exclude manufacture under hospital exemption. IWG are working with the Commission on the responses. Further timelines to be revealed in the future.

Around 20% of contributors that partook in the consultation viewed the production of a self-standing guideline as negative – with concerns around the creation of a double standard in relation to whether ATMPS are produced by industry or academia/hospitals.

Transitional QPs and CTs. Due to some concern over the status of transitional QPs that was identified – the UK national govenance body - MHRA is considering implementing a new reassessment process – to give TQps the opportunityto exhibit how they meet article 49 2 and 3 requirements in regards to IMPS.

In regards to clinical trials this assessment will look at eligibility of the QPs and examine the suitability of any named person to act upon specific manufacturing license. IMP sectors – new entrants would have to go through the permanent provision route.

Interested in sharpening your GMP awareness?

Pharma IQ Quality Training Series

20 – 23 June 2016 | London, Uk

Attendees Will Learn

- To further develop understanding of the core principles of GMP
- To increase understanding of the Chapters and Annexes that constitute the Basic Requirements for Medicinal Products
- To examine the practical application of GMP within the production environment.

www.pharmatraining.co.uk | Call: **+44 (0) 207368 9300**

Email: **Enquire@iqpc.co.uk**

Download the Agenda

Resources

1. http://www.gmp-compliance.org/enews_05203_Outlook-What-will-bring-the-GMP-Year-2016.html


Pharma Logistics IQ
Packaging and Labelling

Pharmaceutical Packaging and Labelling Summit

2016 Trend Report

Perigord
life science artwork solutions

Pharma iQ
a division of IQPC

CONTENTS

FOREWORD

According to recent research, the global pharmaceutical packaging market is forecasted to reach more than US$80 billion in revenue by 2020.

This expanding market is advancing towards optimization in regards to effectiveness. However, as noted in recent research, this wasn't always the case: "Packaging was considered as an afterthought which was required merely in the final stages of manufacturing for many pharmaceutical companies about a decade ago. But of late, pharmaceutical packaging has quickly become an essential part of the drug delivery system.." (1)

Off-patenting drugs, the growing generics industry and the progression seen within manufacturing are all expected to fuel the advancement of the packaging market.

The pharmaceutical packaging and labelling market is predicted to feel a boost from the maturation of the biologics market and its new therapies with pre-filled syringes and parenteral vials forecasted to experience the fastest growth.

Asia and Europe follow North America - the biggest market for packaging and labelling equipment. This is due to strong awareness and healthcare investment within the US. (2) Rising contract manufacturing activities' are due to fuel the rapid growth that is ahead for the Asian market.

Upped demands for primary pharmaceutical containers and for flexible and integrated packaging are due to propel the market's activity also. (2) Although, these surging demands can only be catered for if the relevant pharmaceutical packaging and labelling compliance requirements are met.

With this in mind, the packaging, labelling and artwork divisions of the pharmaceutical market face pressures from a range of directions. These include:

- **Producing efficient packaging streams that are compliant and implemented swiftly at a low cost**
- **Varying country requirements**
- **Effectively adhering to new serialisation guidelines**
- **Refreshed regulations**
- **Controlling demanding overheads**

One challenge is presented by the recently revealed Falsified Medicines Directive (FMD) requirements. After waiting for these regulations to be confirmed, market players are now left with the task of achieving requirements by the allocated deadline. Cross-industry insight is of prime value in this instance, as many are keen to learn from other companies' implementation strategies.

In regards to labelling, one key challenge is navigating around country specific guidelines – especially with the amount of information that is required on a package in ratio to the amount of space available.
In this research report, Pharma IQ explores the trends, both those currently prominent and those which are emerging, within the pharmaceutical packaging and labelling market. Also, Suzanne Ivory, Head of Quality at Perigord provides insight into overcoming artwork obstacles on the route to market.

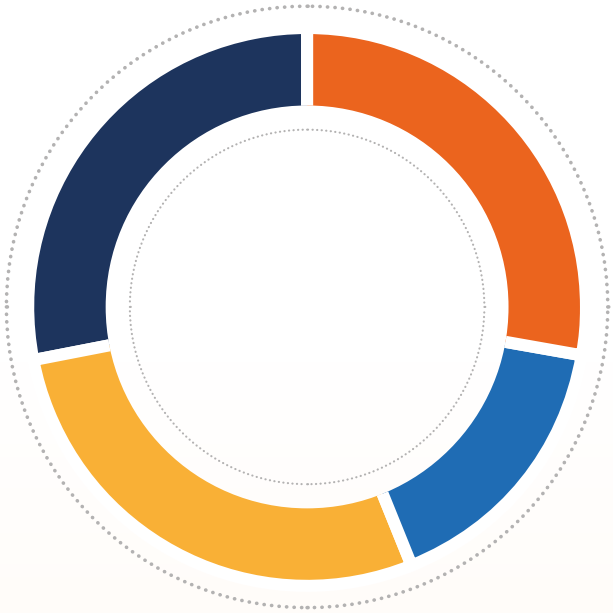
I hope you enjoy

Chanice Henry
Editor of Pharma IQ

ABOUT THIS RESEARCH

Pharma IQ invited its community of pharma and biotech professionals to partake in an online questionnaire in Q1 of 2016 to assess current industry trends in Pharmaceutical Packaging and Labelling industry.

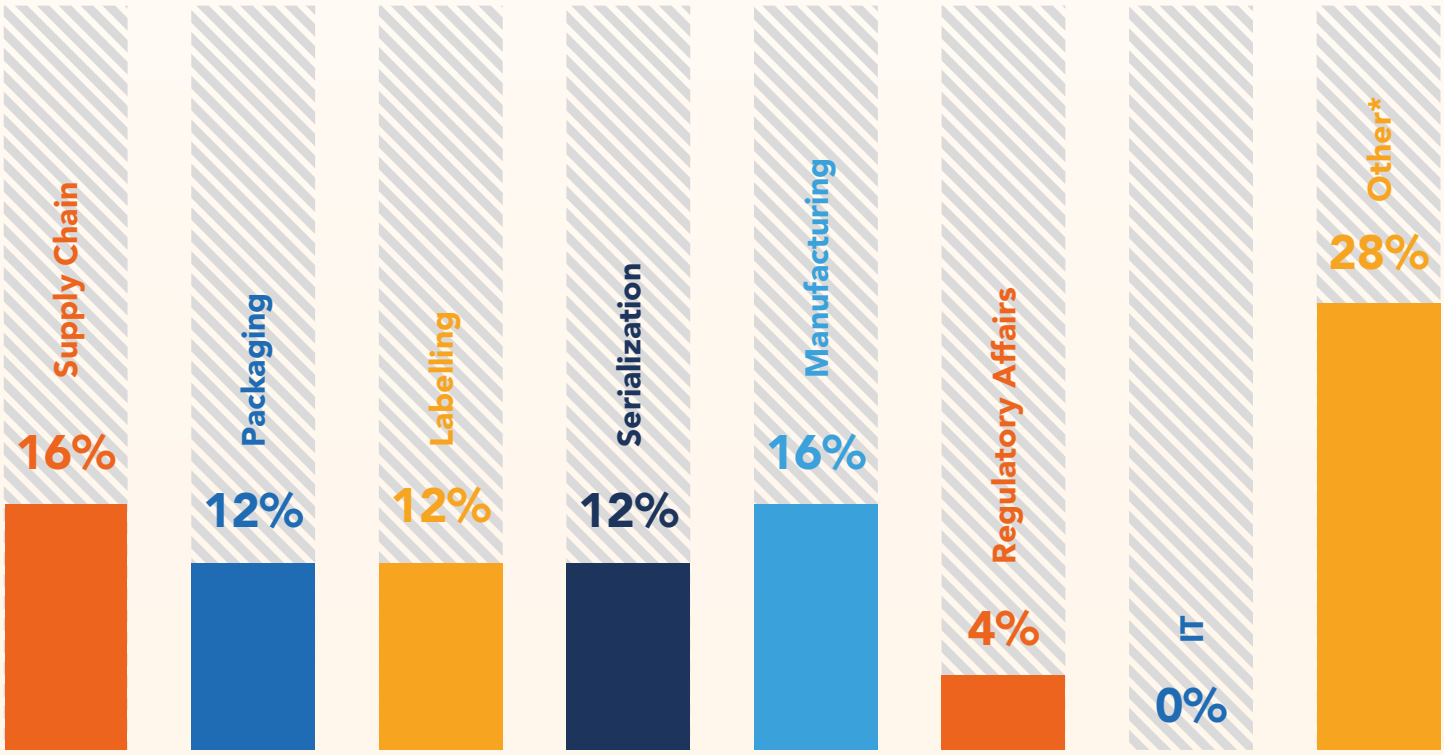
WHAT PROFILE COMPANY ARE YOU FROM?



- Large pharma/bio manufacturer 28%
- Small-to-mid-sized pharma/bio manufacturer 16%
- Medical device manufacturer 0%
- Government 0%
- Solution Provider 28%
- Other* 28%

*Other: Secondary pharma packaging manufacturer, Label manufacturer, Pharmaceutical/MedTech Manufacturer, Wholesaler, OTC manufacturer, small

WHICH FUNCTION DO YOU SIT IN?

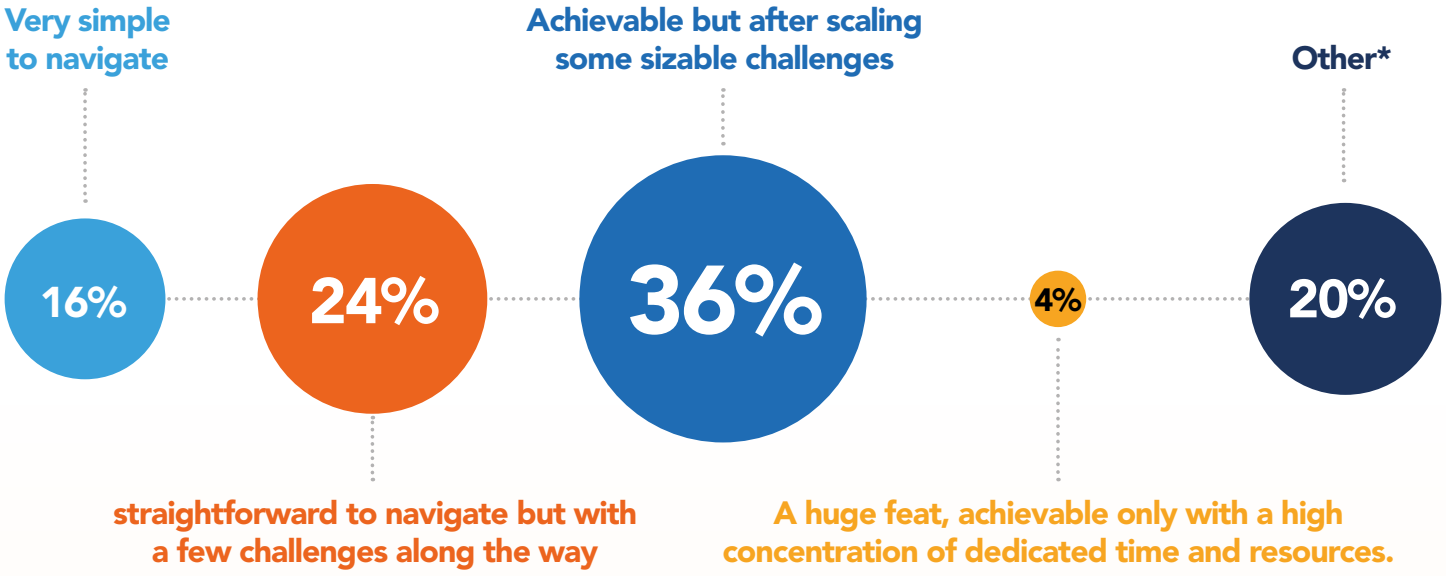


* Consulting Manufacturing and Supply Chain, QA, Product management, Business Development, Implementation Partner

DATA ANALYSIS

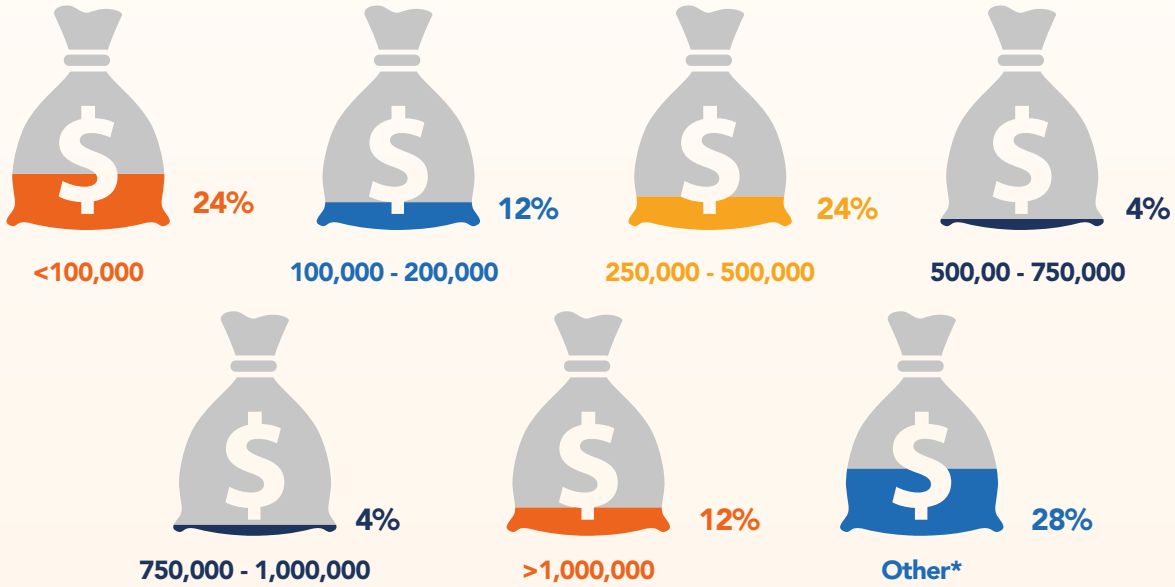
PACKAGING

IN LINE WITH MEETING THE NEEDED FMD DEADLINES – DO YOU THINK YOUR FIRM'S ROUTE TO AIRTIGHT COMPLIANCE IN TERMS OF PACKAGING IS GOING TO BE?



*Other: Clients will underestimate the complexity and effort, Not applicable

HOW MUCH ARE YOU DUE TO INVEST INTO STREAMLINED & EFFICIENT PACKAGING COMPLIANCE OVER THE NEXT 12 MONTHS?

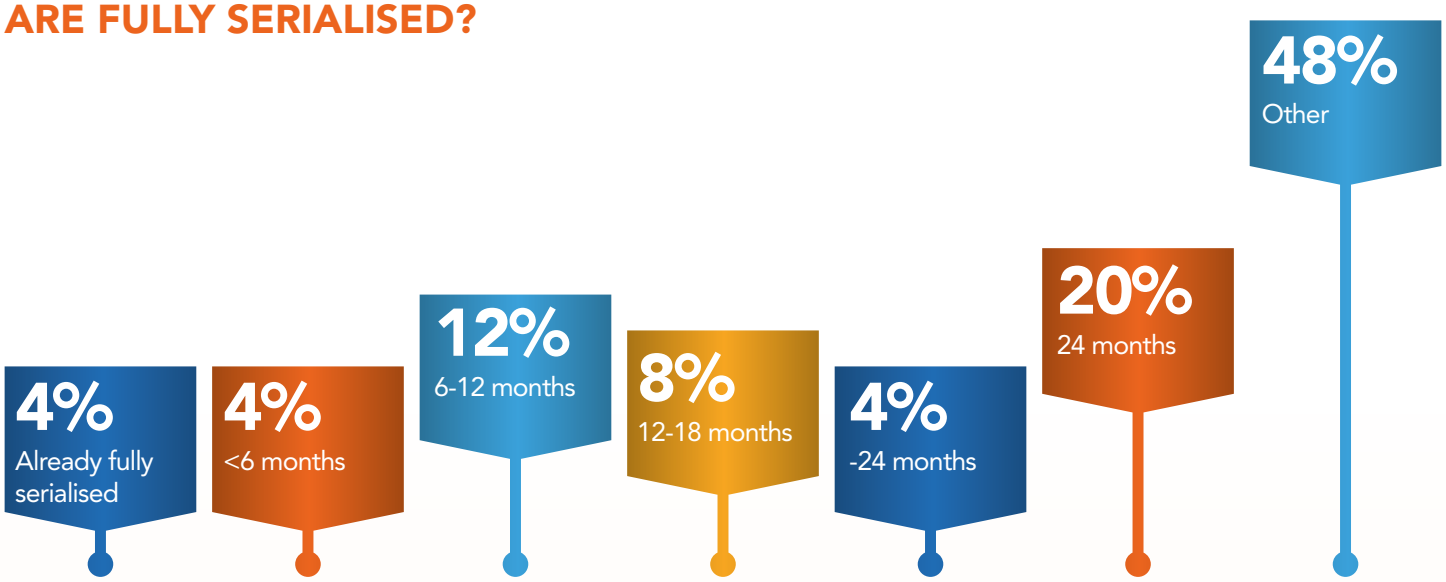


*Other: Not applicable, Not sure dependant upon approvals

After reviewing these results, Dieter Mößner, Project Engineer Pharma, Edelmann GmbH notes a charted confidence in achieving full FMD packaging compliance. In response to the projected investments towards packaging compliance, he perceives that the costs may have been underestimated and participants may have only regarded the direct and external costs and didn't consider not internal costs like project people and training which can be substantial.

SERIALISATION

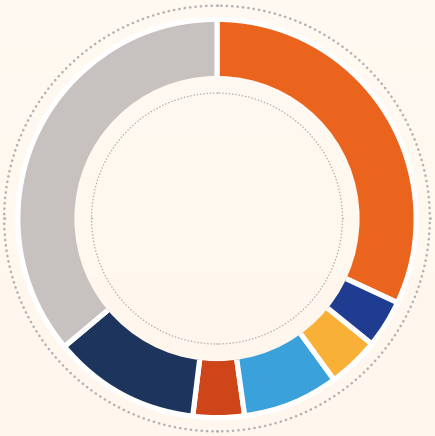
HOW LONG DO YOU ANTICIPATE IT WILL BE UNTIL YOU ARE FULLY SERIALISED?



*Other: Depends on manufacturers, More than 2 years, Time line has not been set yet, Not even started

Only 4 per cent of our participants labelled themselves as fully serialized. Whereas following the 'other category', most people said that they foresaw it would take them around 24 months to reach full serialisation. In Pharma IQ's 2015 research most people said it would take just over 24 months to reach complete their serialisation projects. Surprisingly, some participants noted that a timeline hadn't even been started yet in their organization.

IF APPLICABLE, HOW MANY PACKAGING LINES WILL YOU NEED TO UPGRADE IN RESPONSE TO SERIALISATION?

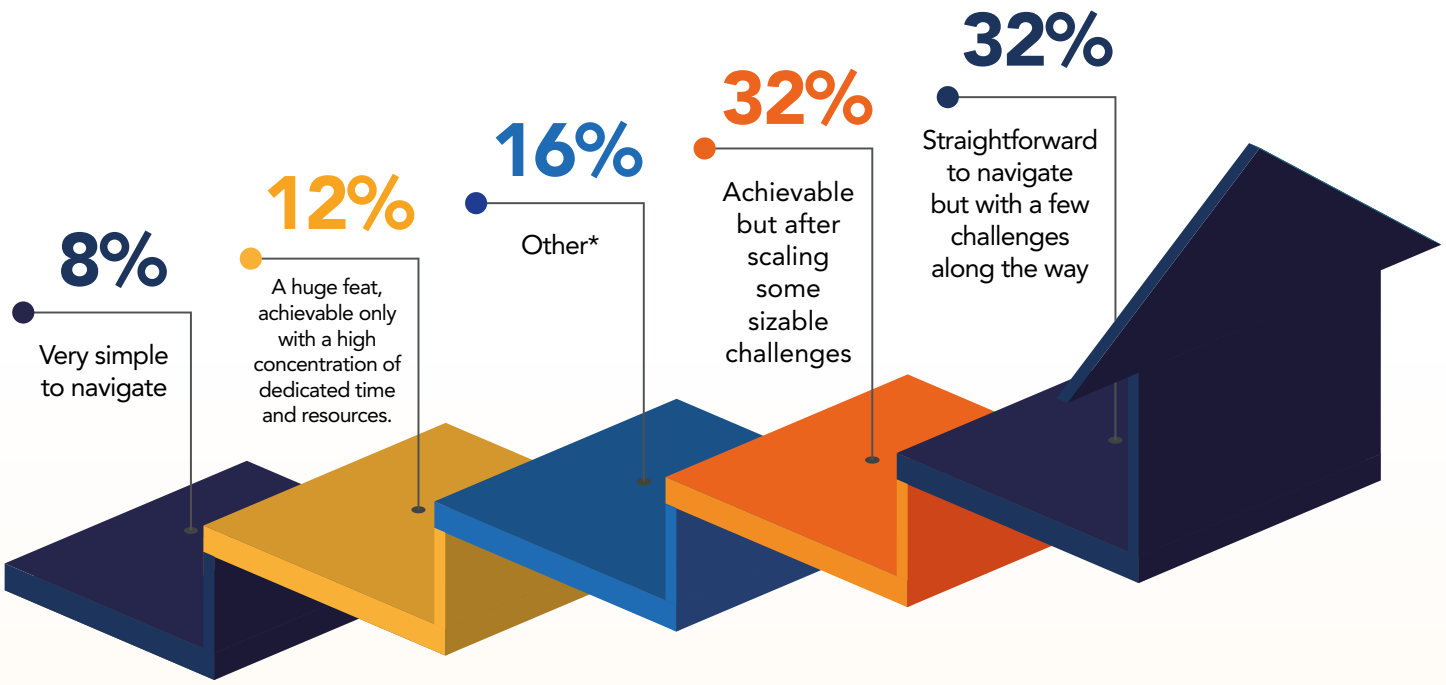


Less than 10	32%
10 – 19	4%
20 – 49	4%
50 – 99	8%
More than 100	4%
Don't know	12%
Other*	36%

*Other: Only need to do pack lines in Serilaisation market scope, Need to design that into the process.

In terms of the amount of packaging lines that need to be upgraded in line with serialisation, a large amount of participants noted that less than 10 lines required attention.

IN LINE WITH MEETING THE REQUIRED FMD DEADLINES – DO YOU THINK YOUR FIRM'S ROUTE TO AIRTIGHT COMPLIANCE IN TERMS OF SERIALISATION IS GOING TO BE?

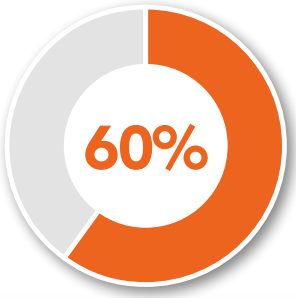


*Other: N/A

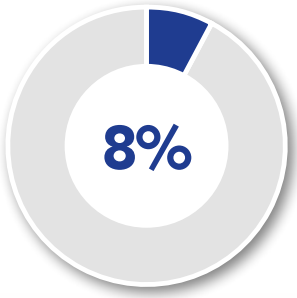
The majority of participants agree that the adherence to FMD deadlines is going to present challenge in someway. With 32% expressing confidence that the route to airtight compliance will be straightforward, another 32% of the research base stated that it will be achievable once some substantial challenges have been navigated. This could be perhaps have a correlation to the size of firms within the research.

LABELLING & ARTWORK

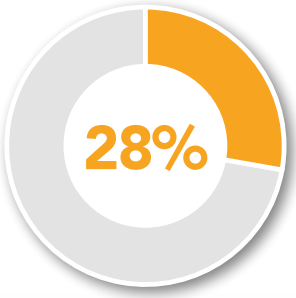
WHAT AREA OF THE COUNTRY SPECIFIC GUIDELINES IN TERMS OF LABELLING USUALLY PRESENTS THE MOST CHALLENGES?



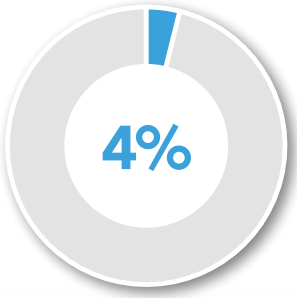
Space for the details required



Anti-Tampering requirements



Translation



Other*

"No particular surprise here about space being the predominant issue. Because it's become an increasing challenge to fit more and more and more content on a small packaging, You don't want to make the carton 2 feet by 3 feet to fit everything on, as it has to be convenient for people to carry.

"If you look at serialisation and tamper evidence that's driving a requirement for even more space because you have to allow space for the serialization code and you need somewhere to put tamper evidence seals, if you choose to use them. So, the regulators are demanding more. The commercial people want more content and you have technical requirements coming through as well now. It's always been a challenge and I think it will always remain to be a challenge.

"The solution to it is to be thinking very carefully early on when deciding the size of the components, what the space requirements are going to be. My view is that ultimately we will be driven away from the huge paper leaflets into booklets before we eventually manage to achieve paperless leaflets, where leaflets are delivered electronically."

Andrew Love, VP Capability Development, Pharma IQ columnist

IN REGARDS TO EFFICIENTLY HANDLING COUNTRY SPECIFIC GUIDELINES, WHICH COUNTRY PRESENTS THE MOST CHALLENGES?

1. Brazil
2. China
3. EU
4. US
5. Asian, Middle and Far East countries
6. Great Britain
7. Canada
8. Latin America
9. Commonly clustered markets e.g. DE/AT/FR/NL/BE/LU
10. Russia

"Those 4 top countries are a large percentage of company sales as they are a big sales market. They have very different requirements across them. And certainly looking at Brazil and China there is quite a lot of change in their regulations, they are evolving quite rapidly.

"From the EU perspective you have got the complication of different types of filing depending on which regulatory approach you are taking, that can drive some complexity. With the FDA there are ongoing changes which come through there – so it doesn't surprise me that those countriescame in as the top four.

"Looking at the Asia Middle East and Far east – what is interesting there is that lots of companies are growing [within these regions].The regulatory environment is again evolving but there is very little commonality between different countries so they are all coming up with their own specific county requirements so it is very difficult to share product between those markets. What you have to do is put in more market specific product which then increases the complexity in the supply chain which people are trying to avoid.

"I could have expected to see Russia higher up the list but that is dependent on how many respondents are really selling product into Russia. But again it is a very fluid country at the moment the regulations are evolving, requirements are changing all the time so it can be a difficult market to deal with."

Andrew Love, VP Capability Development, Pharma IQ columnist

WHY ARE SIMPLE AUTOMATED TRANSLATION SYSTEMS NOT SUFFICIENT TO OVERCOME THE MULTI-LINGUAL CHALLENGES PRESENTED BY A GLOBAL MARKETPLACE?

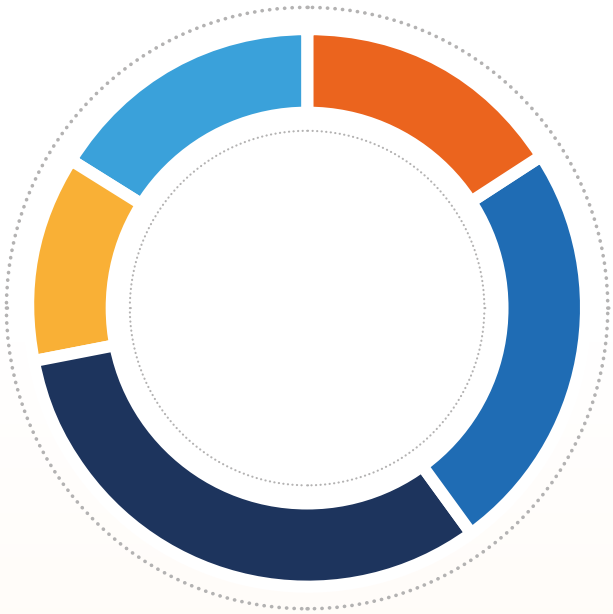
"The points here cover very well the issues using automated translation. The nuances about language can have a big impact on how people read it. And an electronic translation doesn't necessarily have that sensitivity.

Companies that have looked into this a lot have found that a lot of language is product specific. We all dream of a world where the regulatory person can put in the English language and then automatically the artwork is updated in all the different languages through a translation engine and automatic artwork creation. The translation side of that is very challenging to make happen. If you used an automatic translation generator, I think you would still want to have a native speaker to review that translation to ensure that it flowed and made sense.

People are generally starting to see translations as a bigger risk area. I think this is an area that will get an increasing amount of focus over the next few years."

Andrew Love, VP Capability Development, Pharma IQ columnist

IN LINE WITH MEETING THE REQUIRED FMD DEADLINES – DO YOU THINK YOUR FIRM'S ROUTE TO AIRTIGHT COMPLIANCE IN TERMS OF ARTWORK IS GOING TO BE?



- Very simple to navigate 16%
- Straightforward to navigate but with a few challenges along the way 24%
- Achievable but after scaling some sizable challenges 32%
- A huge feat, achievable only with a high concentration of dedicated time and resources. 12%
- Other* 16%

*Other: N/A

> "If you compare this to the answers given to a similar question earlier in the report in regards to serialisation. There is a marked difference seen in those who chose to select the first answer – very simple to navigate. There are less people saying that Serialization is simple to navigate in comparison to artwork compliance"
>
> Andrew Love, VP Capability Development, Pharma IQ columnist

Perigord
life science artwork solutions

OVERCOMING ARTWORK OBSTACLES ON THE ROUTE TO MARKET

Suzanne Ivory, Head of Quality at **Perigord**

With pharmaceutical regulatory demands advancing at a rapid pace, the task of getting a drug to market quickly is becoming littered with added obstacles.

Pharma IQ speaks to Suzanne Ivory, Global Head of Quality, at Perigord for her insight into the biggest struggles faced by artwork professionals in today's pharmaceutical packaging industry. In addition to this, she provides her strategies for how these hurdles can be beaten.

Please provide some insight into the struggles for the pharmaceutical packaging industry between the focus on commercial success and the need to be compliant?

In order to ensure commercial success, the main focus of our pharmaceutical clients' lies in getting their products to market on time, with the need to remain compliant being present throughout the process. However, the reality of a speedy route to market can be complicated by a number of factors.

From an artwork perspective, some pharmaceutical companies underestimate the amount of effort and complexity that can be involved in getting compliant accurate artwork market-ready, on time. While content and regulatory aspects are accounted for, the process needed to create and approve artwork and the interaction of the many stakeholders often isn't.

The effect of issues such as delays in the approval processes and engineering or regulatory changes are not foreseen and because the process to create artwork is not clearly defined the impact on the cost and timing of having a product ready for market can be significant.

Not having clear brand guidelines depicting the positioning of information can result in incorrect artwork or a delay in the approval. For example, the ability to update a leaflet or a carton is greatly complicated if the additional details, be them compliance-led or content-led, cannot fit on the packaging for each market and language.

Therefore, it is critical that this section of the supply chain is managed properly and documented. By ensuring that the artwork process is clearly defined, the integration and communication lines of each stakeholder is clear and that there is complete ownership on the development of the artwork and obtaining swift approval, pharma companies can have a substantial influence on their own commercial success.

What are the costs of not getting packaging and artwork right first time on both a commercial and a compliance level?

When pharma product artwork is not executed correctly the first time, we certainly see the commercial impacts it has on clients. Each time an artwork is processed risk is introduced, and the number of approval cycles subsequently created can have major cost and time implication, but more importantly from a compliance and quality perspective – incorrect artwork can pose a threat to patient safety and so the influence of incorrect packaging stretches far beyond the costly financial implications.

It's crucial that the artwork process is managed with patient safety in mind and not just as a minor part of a packaging chain. The artwork, in the form of patient information leaflets, labels and cartons, indicates how a drug is used. The packaging instructs health practitioners and patients on how to use the product correctly and this is where the strength of the product is displayed. The accuracy of these aspects can be jeopardized if companies don't understand the artwork processes applied when creating products of varying strengths, for example, is one carton used as the basis to create the rest? If so what are the risk factors and how are they mitigated? In a lot of cases content can be correct but a lack of understanding on how versions are managed can still lead to the use of incorrect artwork and in turn a product recall.

In line with being fully focused on patient safety, artwork has to be thoroughly evaluated and pharma companies have to know the hotspots where errors can happen. We see big gaps in the industry when it comes to artwork departments having robust and efficient end-to-end quality management systems.

How big of an issue is this end-to-end awareness for the industry?

It's a huge issue for the industry. I regularly attend and speak at pharma packaging conferences in the USA and EU and get a lot of feedback on this issue from the conference participants and also our clients. When we ask conference audiences: 'How many companies understand and have analysed the artwork process from end to end?' we don't get a huge amount of people confirming that this has been done. Regardless of whether artwork is managed and created in-house or by an external supplier they should clearly define and understand the process from the content stage through to the delivery of printed product. This visibility is so important to a pharma company. They need to understand where the process is managed, by whom, where the approvals take place and where improvements can be made. In obtaining this visibility, it often becomes apparent that old processes are in place that need drastic review.

Regulatory professionals need to understand why they're approving at certain stages so they are able to pinpoint any mistakes. For instance, several different people could be conducting approvals at varying stages between engineering, marketing, quality, regulatory, technical and printing personnel. However, these individuals will not always know the reasons why the approval is being done at that stage or what happens after their stage. The more times an artwork is touched, the higher level of risk associated with the process. In this regard, a system should be deployed that limits the amount of cycles from an internal approval and an external approval process.

The market influences and impacts seen from product proliferation, serialization and safety changes required on packaging have compounded the need for industry players to have the highly efficient artwork processes and quality systems in place.

What are the key things to keep in mind when looking to solve this visibility complication?

It's important to fully understand who the stakeholders are and what their exact objectives are. Aspects to consider when optimizing an artwork process include:

- Is the present process kept in-house or is it outsourced? In the case of the latter, who has ownership and control on the artwork?
- In terms of technologies being used, which ones are impacting the artwork process and what other technologies are available?
- Are there defined procedures in place for managing the artwork workflow including version control.
- Are all the approval stage objectives understood? E.g. when a final approved file is issued to the printer can any changes be made – if so, why?
- Are there specific work instructions in place detailing how artwork is completed?
- Does the Artwork studio have a comprehensive quality management system?
- Which parts of the process can be automated?
- What KPI metrics are being recorded? Is there a detailed analysis completed on internal and external Right First Time?
- What inspection technologies and process are in place and from a metrics perspective how effective are they? When was the process last reviewed in line with changing complexities of artwork?

The creation of detailed and transparent metrics from considerations similar to the above can greatly assist with implementing a continuous improvement program.

Industry analysts have noted that the regulatory realm is likely to remain ever evolving, how can pharma company's stay on top of the task of remaining compliant? – is there ever a way of future proofing a strategy?

In comparison to previous years, there is indeed a higher level of market changes impacting product artwork. Product proliferation has caused the industry to oversee a much higher volume of products. Serialisation requires amends to be applied to a large amount of cartons so codes can be applied. Also, a lot of rebranding is occurring in the market due to various mergers and acquisitions. So, if pharma companies do not have an efficient way of adhering to these advancements, like using an artwork management system for example, they are likely to find the current market climate difficult.

A few years ago, artwork management systems were seen as merely very beneficial. Now, they are an absolute necessity. It's very difficult to have a manual process that allows pharma companies to accurately manage artwork. Adequate folder structures are advantageous, but without a robust artwork management system that ensures only the right version is available to the right people at the right time, pharma companies will discover it's very difficult to grow or to even handle the demands of today's market changes.

The chosen artwork management system must be highly configurable in nature. In theory, having a system that's configurable allows pharma companies, not only to work within their current markets, but also in those which they plan to operate within. The key to being future proofed is to adopt systems that can be integrated and are not purchased on a standalone basis to solve one problem. An artwork management system needs to allow integration into software comparison systems and ERP systems for example. There has to be a direct link across processes so each stage does not stand as an individual event.

The rising popularity of this holistic workflow approach is evidenced by the main buzzword we hear in the market as of late, which is 'end-to-end labelling'. This entails the management of labelling from the creation of Core Data Sheets through each market label. So, in obtaining this approach, if operating software is configurable, the pharma company will be able to sidestep complexity and validation costs associated with changes needed to update the systems.

Finally, any predictions for the future of the packaging and labelling industry?

The artwork side of packaging is ever-evolving, it's probably one of the most technically advanced areas within the packaging supply chain. There are constantly new ways to approach artwork with new automations emerging and it takes the pharmaceutical companies a while to see how beneficial these new methods actually are. It's important for industry stakeholders to stay informed of the available technologies and ensure that the selected software matches their processes as this will help them counter the challenges that lie ahead.

Perigord will be present at June's Pharmaceutical Packaging and Labelling Conference in Geneva. On site you will have the opportunity to visit their stand and attend to their session focused on The Need for Quality Management and Process Control in a Pharma Artwork Studio.

Closing Remarks

The most popular response to meeting FMD regulations in terms of packaging requirements, was that even though the task is achievable, a few large hurdles will obstruct the route to full compliance. Some investment is planned for the area of packaging compliance, with most individuals noting that up to £100,000 would be dedicated to this purpose.

A majority of our participants have initiated their serialisation programmes, with some even stating that they are fully compliant. However, other individuals noted that a timescale hadn't even been set for this implementation.

As expected, space for required materials came out as the top challenge for labelling. In regards to country specific guidelines, Brazil and China were noted as the countries which present the most challenges – which may be related to the recent delay of the finalization of their pharmaceutical packaging requirements.

Despite the challenges that lie on the road ahead, the research results here note a lot of activity scheduled for pharmaceutical and packaging industries.

ACKNOWLEDGEMENTS

Pharma IQ would like to express thanks to all those who participated in this research report and helped in its analysis. A special thanks to Perigord who assisted in the creation of this report.

RESOURCES

1. http://www.marketsandmarkets.com/Market-Reports/pharmaceutical-packaging-market-890.html
2. http://www.medgadget.com/2016/03/global-industry-analysis-on-pharmaceutical-packaging-equipment-market-2014-2020.html

- Top tips –

Improving patient compliance via Packaging and Labelling

Pharma iQ
a division of IQPC

Pharmaceutical Packaging and Labelling Summit

The packaging, labelling and artwork division of the pharma market faces pressure from a range of directions. Varying country requirements, refreshed regulations, controlling the demanding overheads and arguably the one of the most costly pressures is the combat against pharmaceutical inappropriate use by patients. Pharmaceuticals taken incorrectly are a public safety concern, leading to a significant level of fatalities each year.

In regards to enhancing patient compliance, many have noted that behavioral changes are needed not only within patients but the doctors and pharmacists also. One area of recent focus has been combatting the pre-emptive or cautionary admission of antibiotics to patients which is understood to lead to their ineffectiveness in the long term.

Pharmaceutical packaging has a direct influence on patient compliance with medicinal therapy. As explained by Tassilo Korab in a commentary article: "Drug packaging can either build barriers between the patient and the medicine, or can enhance compliance by incorporating features and functions that help patients follow the therapy plan." [4]

After consulting the expertise of packaging specialist Karel van der Waarde Pharma IQ presents its top tips to reducing patient pharmaceutical misuse via packaging and labelling.

1 Enroll patients into the packaging design process

One prominent tactic to combat patient inappropriate use is the consultation of public opinion on the development of packaging design in regards to how it can better enable patients to take medicines appropriately.

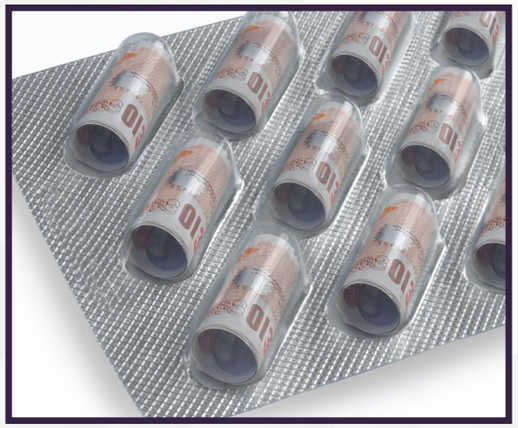
In this case, Karel van der Waarde explained: "You go to real patients and ask them and interview them and see how they work in real life with your packaging. [For example] see what problems elderly people have with opening of a cardboard box and look at how arthritic patients work [with] tablets."

He noted that via this analysis, intelligence may be uncovered that can assist with design to optimise patient compliance. For example, providing discrete labelling to medicines which are therapeutics for conditions that can invite social stigma - such as HIV medicines.

This level of user analysis is likely to require the input from all ends of the market: legal groups, the industry, patients, doctors and pharmacists. In this regard legislation may also require improvement or amendment to ensure that this can be done compliantly.

2 Strike a balance between anti tamper and usability

In regards to the latest FMD EU regulation, Karel notes that he has seen some fully compliant packaging, however their compliance has triggered some usability problems. This comes with the robust transparent tape used to seal the box and the package leaflets also. These have especially been causing usability issues with elderly or patients with arthritis or sight impairments who are unable to break and sometimes even see the tape. Karel concludes that as well as remaining compliant in packaging, the pharmaceutical industry needs to conduct usability tests.



3 Artwork inaccuracies are not an option, due to:

Their influence upon misuse by patients

Artwork errors can range from:
- The complete omission of a vital piece of information from artwork
- The ambiguous presentation of information which can lead to miscomprehension

- Incorrect symbols
- Technical errors – for instance serialisation code or barcode. [5]

Patients rely on the information provided on a product to instruct them in a manner which will lead to safe and effective use. Therefore any flout in accuracy could have fatal consequences. Also this could damage the wider confidence in the treatments themselves - which would be hard to replenish.

Their influence upon misuse by pharmacists

As physicians trusted with restoring patients to health, these professionals - which have hectic workloads - rely on the packaging and labelling of a product being fit for purpose. An error in regards to the information supplied on a package could result in a prescribed medicine having a negative influence on the patient. In addition to this, it would be a drain on resources for these physicians to dedicate time and money on rectifying or consciously avoiding issues created by packaging and labelling errors. [4]

4 Avoid Chinese Whispers In The Chain From Doctor To Pharmacist To Leaflet

One major inefficiency is in regards to the variety of information given to patients for one pharmaceutical. Sometimes the information provided by doctors, pharmacists and the product's literature can differ – which could skew the usage of the medicine itself. Karel van der Waarde urged that there needs to be a focus on ensuring there are exact parallels in the information given from different sources on one product. This is especially important with patients that need to take a selection of drugs safely.

5 Tailor design to the safety of the end user in focus

Karel van der Waarde notes that packaging should be sufficiently aligned to the safety profile of a pharmaceutical.

In regards to the medicine type…

- Highly Addictive
- Too complex to be combined with other medicines.

Also, in regards to the user type….

- Pregnant women
- Children
- Parents who need to keep the product safe from children.
- Pharmacists, doctors and professors.

In regards to patient safety Karel notes that the cases and situations of focus need to be considered and catered. This would optimise the patient's compliance in a wide range of circumstances.

Instead of producing information for a therapeutic medicine at one level, information should be aimed to be provided on varying levels and through a range of platforms and media. Of course legislation needs to accommodate for these improvements.

6 Customise the packaging information to the stage of the condition

Currently for those with chronic diseases, a patient could be receiving the same information about a product for 30 years. Packaging information tailored to the stage of the condition at hand could move to sustainably optimise patient compliance with medical products.

7 Deploy An Artwork Governance Team

A refined focus on packaging and labelling will help minimise mistakes and could even optimise patient use of a pharmaceutical. An artwork governance team is equipped to manage the delivery of artwork and will consider contributions from all relevant stakeholders. Amongst its responsibilities to administer quality control, the team would outline the packaging and labelling strategy and monitor its implementation.

Karel van der Waarde is going to be present at the 2016 packaging and labelling summit in June.

Resources

1. http://www.businesswire.com/news/home/20160225005055/en/Growing-Disposable-Medical-Products-Significantly-Augment-Market
2. http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm220112.htm
3. http://ec.europa.eu/health/newsletter/140/focus_newsletter_en.htm
4. http://www.samedanltd.com/magazine/15/issue/78/article/1766
5. http://www.pharmaceuticalonline.com/doc/packaging-artwork-errors-to-avoid-and-their-implications-0001
6. http://www.pharmaceuticalonline.com/doc/establishing-a-service-culture-for-your-labeling-and-artwork-0001


Pharma Logistics IQ
Stay Tuned
Newsletters are published on Wednesdays