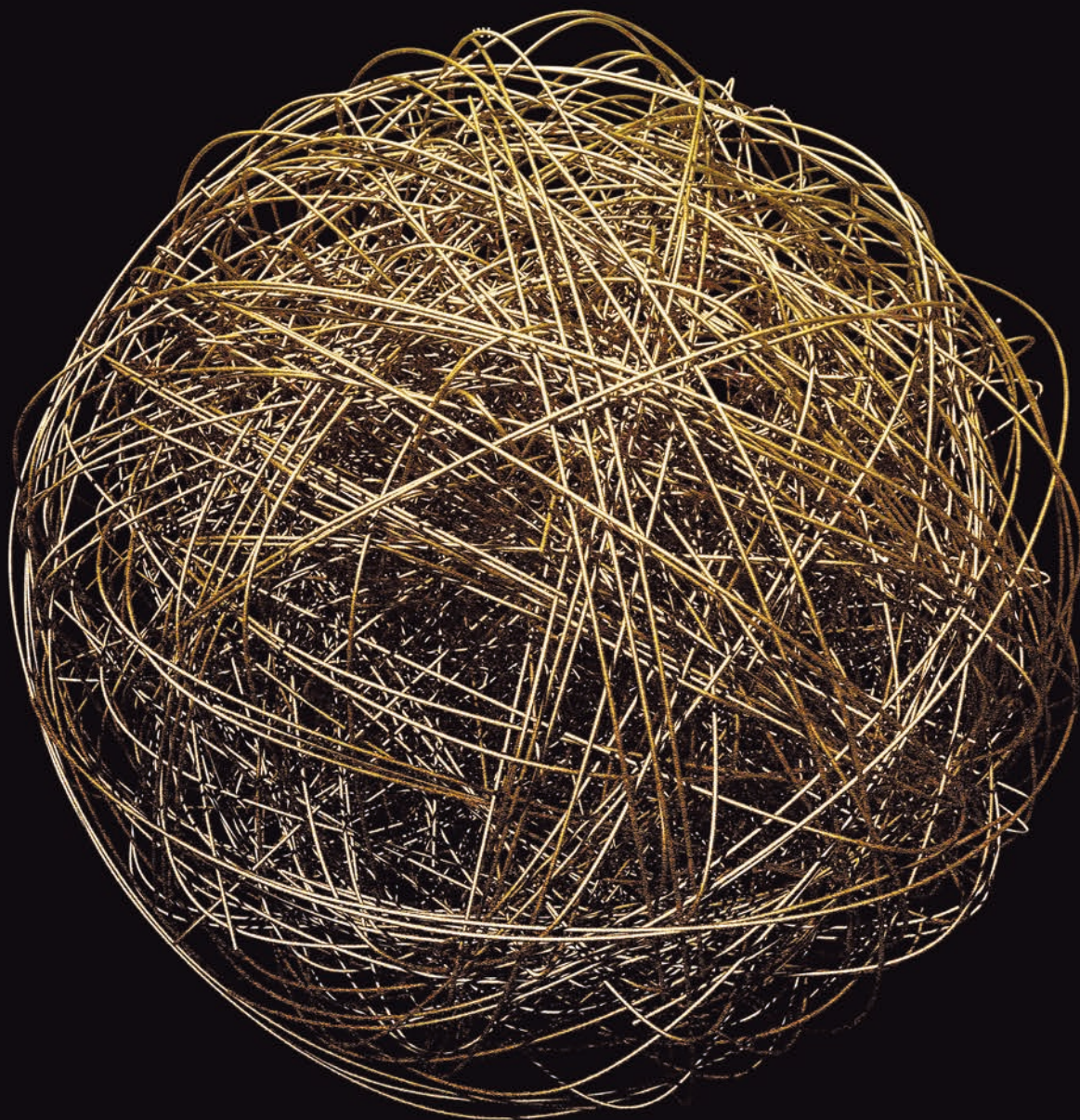


Deloitte.



Unravelling complexity

The challenge of compliance in
the life sciences supply chain

April 2017

Deloitte Centre *for*
Health Solutions

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The Deloitte Centre for Health Solutions

The Deloitte UK Centre for Health Solutions is the research arm of Deloitte LLP's healthcare and life sciences practices. Our goal is to identify emerging trends, challenges, opportunities and examples of good practice, based on primary and secondary research and rigorous analysis.

The Centre's team of researchers seeks to be a trusted source of relevant, timely, and reliable insights that encourage collaboration across the health value chain, connecting the public and private sectors, health providers and purchasers, patients and suppliers.

Our aim is to bring you unique perspectives to support you in the role you play in driving better health outcomes, sustaining a strong health economy and enhancing the reputation of our industry. In this publication, references to Deloitte are references to Deloitte LLP, the UK member firm of DTTL.

Foreword

Welcome to the Deloitte UK Centre for Health Solutions' report *Unravelling complexity: The challenge of compliance in the life sciences supply chain*.

The life sciences industry operates in one of the world's most regulated environments. Global life sciences supply chains are lengthy and complex, shaped by many internal and external factors. To retain their licence to operate, companies must comply with an evolving set of global laws and regulations. Failures of any kind in the supply chain are hugely damaging to them in terms of immediate loss of revenue from delayed product launches, remediation costs and long-term reputational damage. Importantly, the impact is often felt more broadly in the healthcare system. Shortages of medicines and other key products, as well as the risk to product quality, have a profound adverse effect on patients' lives.

In November 2015 we published an overview report – *The Challenge of compliance in life sciences: Moving from cost to value*. This explored the challenges that life sciences companies face in responding to an increasingly complex global regulatory environment. This second report continues our focus on compliance through an in-depth evaluation of the key regulatory challenges in the life sciences supply chain and potential solutions.

The findings in this report draw on the experience of Deloitte life sciences supply chain and regulatory specialists, literature reviews and insights gained through interviews with senior industry leaders who are accountable for establishing, operating and auditing life sciences supply chains.

We hope our assessment provides new ideas and suggestions for tackling the current and future regulatory challenges in the life sciences supply chain, and we welcome your views and feedback.

John Morgan
Director
Healthcare & Life Sciences

Karen Taylor
Director
Centre for Health Solutions

Executive summary

The life sciences industry strives to deliver products to patients in a complex environment driven by mounting regulatory scrutiny, globalisation, alliances and partnerships, mergers and acquisitions, escalating pricing pressures and eroding profit margins. To address these challenges, companies are looking to their supply chains to deliver products to customers, while also maintaining regulatory compliance. A safe, reliable, cost-effective supply chain is critical to value creation.

This report is a follow-up to our previous report on *The Challenge of compliance in life sciences: Moving from cost to value*. Its focus is on the critical role of the global supply chain and the industry's ability to comply with a highly complex and evolving set of rules and regulations. Based on literature reviews and in-depth interviews with senior supply chain and compliance leaders in ten major life science companies, this report also draws on Deloitte's extensive experience working with the industry. It sets out five key regulatory challenges which impact the supply chain and five actions to help address these challenges.

Supply chains are traditionally linear, but they are now transforming into dynamic, interconnected systems. Life sciences supply chains extend from multiple tiers of procurement, manufacturing and testing sites to global, regional and in-market storage and distribution units. Indeed, the supply chain is the golden thread that links discovery to delivery within the life sciences value chain.

Today's life sciences company has an increasingly fluid and innovative product portfolio and operates in a growing number of developed and developing markets. As a result the supply chain is increasing in complexity at the same time as scrutiny from national and international regulators is intensifying. The compliance capabilities of the industry are being tested by the need to interpret and comply with existing and emerging legislation and implement any necessary changes to the supply chain in response to these regulations in a co-ordinated, cost-effective and timely manner. Getting it right can be a source of competitive advantage.

Key challenges for supply chain compliance are:

- **meaningful measurement** – measuring compliance is complex and lacks comprehensive metrics to achieve visibility of compliance status and risks across the end-to-end supply chain
- **supply chain complexity** – this highly complex environment is driven by the impact of intellectual property, tax structures and changing market access needs, as well as a growing reliance on third-party business partners, requiring effective governance and risk management
- **the complexity of new product types and therapies** – products are more diverse and have shorter product lifecycles, and there is a growing emphasis on outcomes and new models of healthcare delivery
- **implementing changes within existing regulatory frameworks** – the management of regulatory and technical change presents a significant cost and operating challenge for life sciences companies.
- **the increased pace of regulatory changes** – the proliferation of new regulations is set to continue, and regulators are increasing their compliance oversight and enforcement activities.

To address these compliance challenges, we have identified five key actions:

Develop an ethics driven culture through effective leadership and governance

Companies across the industry have acknowledged the importance of developing an effective compliance culture. At the same time, regulators are intensifying their scrutiny of each company's compliance culture as part of their inspections. The culture of a life sciences company, which is driven from the top down, needs to support decisions that are right for compliance and right for the business. Moreover, as our previous report on compliance found, to ensure ethical behaviours and that employees act with integrity as the norm, the 'tone in the middle' needs to gain as much emphasis as the 'tone at the top'. Life sciences companies should take a proactive approach to diagnosing the core values and behaviours that serve as their cultural foundation and develop a vision and roadmap that leads to a high-performing sustainable culture committed to improving compliance.

Extract greater value from data

Life sciences companies generate huge volumes of data in order to maintain the efficiency and cost-effectiveness of their supply chain operation. However the use of data is often siloed with data systems fragmented between compliance and operational systems. 'Big data' and analytics will be a key enabler in unlocking the potential that these disparate sources of data can provide and should improve the ability of companies to identify and quantify new and emerging risks. Data analytics is increasingly sophisticated and could be used more effectively to drive compliance and enable a better understanding of key supply chain risks. Predictive compliance risk management will rapidly become a new and distinctive capability.

Understand the costs and benefits of investment in supply chain compliance, talent development and/or outsourcing

Many life sciences companies maintain large and growing compliance functions at significant operational cost to ensure they maintain regulatory compliance. Companies are now beginning to examine these costs more closely and are exploring alternative approaches to performing these operations such as using third parties. Although this may increase risk by placing their "right to play" with an outsource provider, it may nevertheless be the most suitable approach where there are skills shortages in the market.

Build a balanced relationship with regulators including supporting regulators to develop greater regulatory harmonisation

As life sciences companies continue to expand their global commercial and manufacturing footprint the demands on regulators are also increasing, forcing regulators to re-think their approach to how they regulate the industry and the role that they should play. Greater harmonisation between regulators is increasingly seen as a key enabler in maintaining compliance while securing supply to markets. Industry can help by developing collaborative relationships with regulators, working with them to predict and manage regulatory risk and compliance, proactively. Regulators have a huge volume of documentation to respond to, and industry can help to optimise the management of this documentation. By building engagement with regulators into their innovation models, new regulations for innovative treatments, such as 3D printing of drugs or gene editing, can be developed contemporaneously rather than retrospectively using enhanced regulatory pathways.

Adopt digital technology, including robotic process automation

There is significant potential for life sciences companies to take advantage of the exponential growth of data analytics, cognitive computing, connectivity and new technologies to transform the traditional linear and siloed supply chain processes into 'Digital Supply Networks'. These networks can harness the flow of information, goods and services between the physical and digital worlds, providing visibility into the extended supply chain, including third party business partners and outlying operations. Advanced cognitive technologies can leverage large volumes of data and identify and even predict complex compliance challenges. Many of the supply chain compliance processes are routine, lending them well to optimisation through robotics (software algorithms) and machine learning. This can not only reduce costs but also improve the accuracy, resilience and the reliability of supply chain compliance.

Conclusion

Supply chains evolve over time, and the coming years are likely to see dramatic transformation due to the combination of accelerating technology development and widespread adoption of new operating and business models. Regardless of the approach taken, a well-designed programme for supply chain compliance will provide an effective and holistic model for companies to discover, prepare, analyse, and respond to existing and emerging supply chain compliance risks and requirements. A scalable and flexible solution that leverages advanced analytics and robotics will enable companies to adapt to and proactively monitor compliance challenges in today's evolving supply chain environment.

The life sciences supply chain

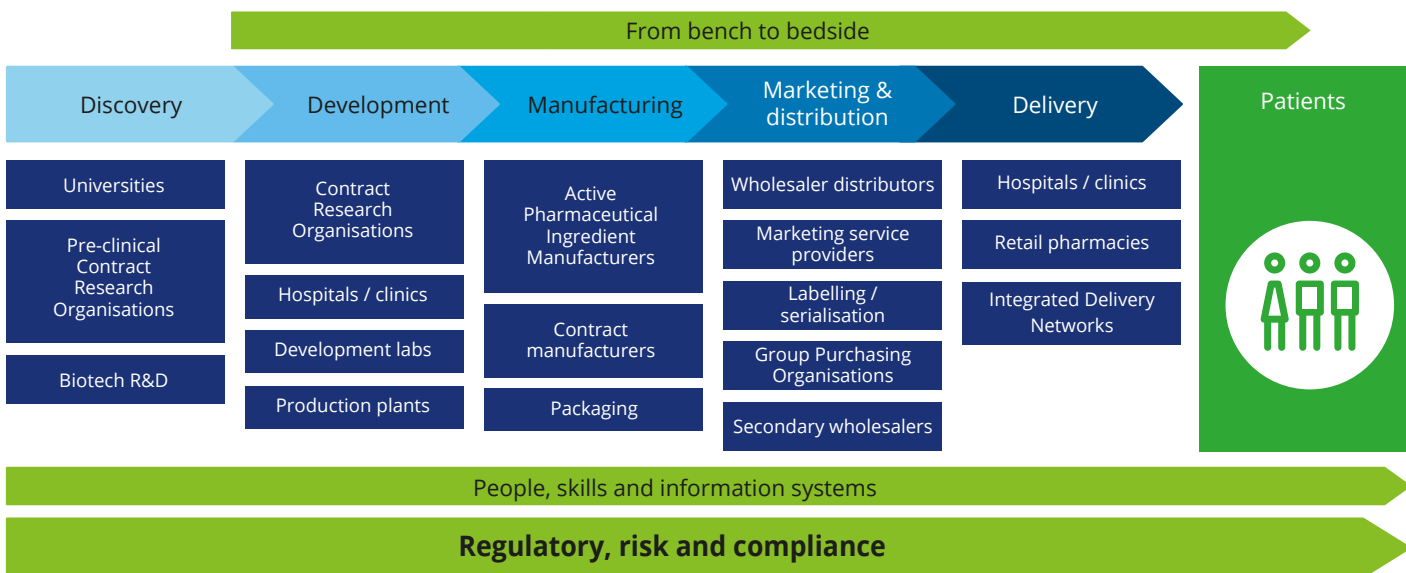
The life sciences industry is facing significant cost and pricing pressures and is undergoing dramatic changes in its operating environment. These include: further globalisation; more alliances and partnerships; heightened transparency expectations; an increased emphasis on innovative technologies; convergence between the medical technology and pharmaceutical industries; and a proliferation of regulatory changes. This has added to the complexity of the life sciences supply chain, escalating the importance of ensuring that all products are manufactured, distributed and delivered in a safe, cost-effective and timely manner.

In November 2015, we published a report on the challenges life sciences companies face in responding to an increasingly complex regulatory environment while, at the same time, ensuring a strategic balance between compliance risk and value. Our report, *The challenge of compliance in life sciences: Moving from cost to value*, identified seven key insights:

- life sciences companies often lack an enterprise-wide view of compliance risks
- applying advanced analytics to 'big data' can help identify and quantify new and emerging risks
- an ethics-driven culture can provide a competitive advantage for companies, with 'tone in the middle' as important, if not more important, than 'tone at the top'
- companies with the most mature compliance functions that focus on developing the compliance skills of employees will win the talent war
- a significant risk for global companies is a lack of dedicated compliance resources in local markets
- major opportunities exist to optimise compliance by deploying continuous readiness models, combined with risk assessments
- the industry needs to develop a balanced position with regulators, leading companies build regulatory engagement into their innovation models.¹

In publishing the first report, we emphasised that our research was ongoing and that subsequent report(s) would focus on solutions that could enable life sciences companies to optimise their compliance functions. This follow-up report focuses on the challenge life sciences companies' face in managing regulatory compliance across their increasingly complex and diverse supply chains.

Figure 1. Life sciences supply chain - linking discovery to delivery across the life sciences value chain



Source: Deloitte

The complexity of the supply chain

Life sciences supply chains extend from multiple sources of procurement, through multiple stages of manufacturing and testing to global, regional and in-market storage and distribution (Figure 1). Indeed, the supply chain is the golden thread that links discovery to delivery within the life sciences value chain.

Over the past decade, the life sciences industry has experienced increasing competition, expiring patents, slowing sales growth, and declining profitability. As a result, companies have focussed their attention on maintaining a healthy R&D pipeline and improving the efficiency and effectiveness of discovery, research and asset development. Increasingly, companies have also turned to mergers and acquisitions (M&A), joint ventures and other partnership models. Life sciences companies now have a more fluid product portfolio, with novel technologies, combination therapies and drug/device combinations. The result is a supply chain for developing, manufacturing and distributing pharmaceuticals and medical devices that is highly complex.

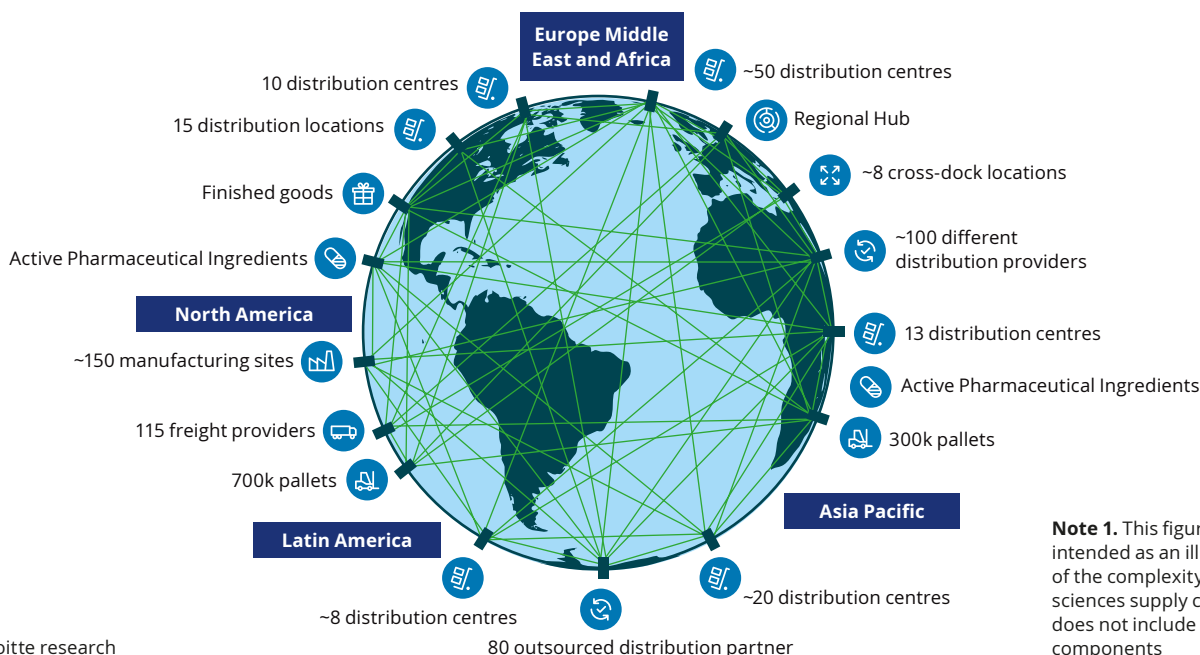
Trends driving supply chain complexity include:

- sourcing of active pharmaceutical ingredients (API) and raw materials from low cost countries²
- a shift in pharmaceutical product portfolios from blockbuster small molecule therapies to large molecule therapies and smaller patient populations, often requiring specialised manufacturing technologies, impacting the size and scale of global production facilities³
- more extensive use of external contract development and manufacturing organisations (CDMO) to avoid fixed asset investment risk, improve agility and enable access to ready-built capacity and innovative manufacturing technologies
- the emergence of direct distribution models and expansion into new markets, shifting the role of logistics service providers (and, in some cases, wholesalers) to be a more integral part of a life sciences company's sales and delivery operations

- accelerated approvals of breakthrough therapies, giving companies less time to establish product supply chains
- intellectual property rights, tax structures and changing market access needs which are creating new imperatives for supply chains.

Figure 2 shows a typical globally distributed network consisting of hundreds or even thousands of constituent parts (nodes), supporting a complex web of global product flows within the supply chain. Many of these nodes are operating thousands of miles from oversight by corporate head-quarters, and each is governed by its own set of comprehensive national and international laws and regulations.

Figure 2. Illustration of the complexity of a globally distributed life sciences network



Note 1. This figure is intended as an illustration of the complexity of a life sciences supply chain and does not include all of the components

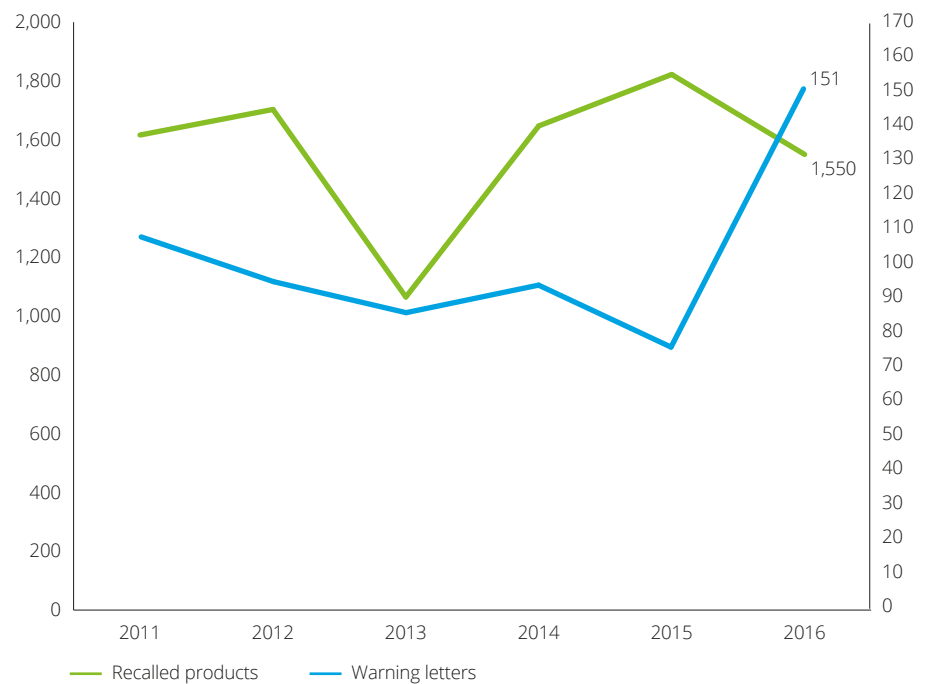
The importance of compliance in the increasingly complex supply chain

A safe, reliable, efficient and cost-effective supply chain is critical to both business success and delivering outcomes to patients, while having to comply with a highly complex and evolving set of rules and regulations. The growing reliance on third parties, globalisation and supplier consolidation, coupled with heightened regulatory enforcement, are increasing overall supply chain risk.

Compliance issues, not only within a company's managed facility but also suppliers' and contractors' facilities, can be hugely disruptive to operations. The consequences for a life sciences company are immediate loss of revenue and/or delayed product launches, costly remediation programmes, fines and long-term reputational damage. For example, recalled products by the FDA Center for Drug Evaluation and Research (CDER) have remained high over the past six years with a peak in 2015.⁴ Recalls are not only extremely costly but also bring reputational damage to the manufacturer. The number of CDER issued warning letters have also risen with 2016 seeing a 199 per cent rise over the number issued in 2015 (see Figure 3).⁵ Public warning letters can harm a company's reputation and inadequate remediation actions often result in serious enforcement consequences.

Case example 1 illustrates the types of quality system failures and recalls associated with purchased components for medical device companies including the proportion of failures in purchasing controls.⁶

Figure 3. FDA, Centre for Drug Evaluation and Research number of warning letters and product recalls, 2011-16



Source: FDA Enforcement statistics summary of Center for Drug Evaluation and Research (CDER) warning letters and product recalls

Case example 1. Regulatory compliance and the increasing focus on 'Purchasing Controls' when inspecting medical device companies' supply chains

In order to support the FDA's Transparency and Case for Quality Initiatives, the Center for Devices and Radiological Health is supplying data on inspections, inspectional observations and warning letter citations issued in 2015. The FDA believes the information will help the industry improve device quality through the sharing of common inspection observations, identify areas of emerging concern, and help firms avoid receiving warning letters. Growing numbers of recalls associated with purchased components, coupled with the increasing reliance on outsourcing, particularly of key components, has resulted in FDA investigators increasingly focussing on Purchasing Controls during established inspections. Purchasing Controls accounted for 32 per cent of the 3,525 Quality System observations at 2,104 medical device manufacturers inspected worldwide in 2015. Purchasing Controls are now a common starting point during a medical device Quality inspection, along with Corrective and Preventative Action, Complaints, Validation and Audits.

When regulatory failures do occur, they can be very damaging to the integrity and trust agendas in which companies have invested heavily over recent years. These failures have potential consequences for patient health through medicine shortages and, in the case of product quality issues, the potential for adverse events such as harm or even death.

The research methodology for this report

The aims of our research were to evaluate the challenges that life science companies face in attempting to manage supply chain compliance in an increasingly complex and dynamic operating and regulatory environment and identify the actions that companies can take to optimise compliance. Our report findings are based on literature reviews and in-depth interviews with senior leaders responsible for supply chain quality and compliance functions within ten major life sciences companies. We have supplemented these research findings by drawing on the broad experience and insights of Deloitte supply chain and risk and regulatory specialists.

During the interviews, our discussion focussed on product quality and supply chain risk, including good manufacturing, storage and distribution practices specific to the life sciences industry and trade compliance risks that apply more universally across industries. Our interviewees also raised concerns over broader risk areas such as corporate risks (financial compliance, health and safety) and regulatory issues.

What do we mean by supply chain compliance? To ensure consistency in terminology across the respondents' answers we used the definitions based on those outlined in the International Society for Pharmaceutical Engineering (ISPE) Glossary of Pharmaceutical and Biotechnology Terminology.

Supply Chain: The sequence of processes involved in the production and distribution of a commodity. A supply chain normally encompasses new product development; supply of materials to a manufacturer; the manufacturing process; and the distribution of finished goods through a network of distributors and retailers to a final customer. Companies involved in various stages of this process are linked to each other through a supply chain.

Compliance: The practice of obeying rules or requests made by people in authority, e.g., adherence to certain specified standards such as regulations, good practices, standard operating procedures (SOPs), service-level agreements (SLAs), or specified (user) requirements.

The challenge of compliance in the supply chain

The life sciences industry operates in one of the world's most regulated environments.

To maintain a licence to operate, companies must comply with a highly complex set of laws and regulations. Over the life-cycle of a drug, companies must adhere to both commercial compliance such as Anti-bribery and Corruption and specific compliance industry obligations, such as, Good Vigilance Practice (GVP), Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP), which impact the supply chain. It is not only individual laws and regulations that are complex, but also the regulatory landscape, with each country in the world having its own regulatory requirements.

“There are all kinds of authorities: FDA, my local regulators, China and for the first time Turkey, Brazil, South Korea. They follow different directions, and it's difficult to satisfy them all... they may have conflicting requests. It's really, really complex.”

Global Head of Quality

Over the past few years the life sciences industry has faced growing scrutiny from international regulators.

The life sciences industry is also experiencing dynamic shifts in consumer attitudes, such as expecting earlier access to new products. There is also a move towards greater patient engagement, both in determining the effectiveness of a particular therapeutic pathway and its impact on patient adherence, and in obtaining information on patient reported outcomes. Life sciences companies are therefore attempting to balance the strategic objectives of their supply chain operations with the need to meet ever more demanding customer expectations, while also keeping up with the changing regulatory environment.

One of the key findings from our 2015 study was that life sciences companies often lack an enterprise-wide view of compliance risk. Our expectation on entering this second phase of research was that within an individual operational or business function, such as the supply chain, compliance risk should be managed within one discrete compliance agenda. However, it quickly became apparent from our discussions that no one function within a company's supply chain has full visibility of the entirety of compliance risk, with accountability for different aspects of compliance typically split between commercial supply, quality management and regulatory.

“Regulators are asking for ever more documentation that evidences that the right methods are being adhered to – regulatory citations are increasingly focused on data integrity.”

Manufacturing Site Director

We asked interviewees to explain what the challenge of compliance in the supply chain means to them. Initial responses typically focused on meeting rules and regulations and being compliant with country licences. However, in further discussion, it became clear that they recognised that blindly following the rules is not enough and that compliance is much more than a 'checkbox exercise'. One interviewee talked about “finding a smart way” to achieve a balance between regulations and supporting the business. Compliance is therefore more about the spirit and not just the letter of the law. Indeed, regulators and life sciences companies have the same interests at heart – patient safety and products that work.

Our research identified five key challenges:



meaningful measurement



supply chain complexity



the complexity of new product types and therapies



implementing changes within existing regulatory frameworks



the increased pace of regulatory changes

Meaningful measurement

The FDA's Office of Pharmaceutical Quality (OPQ) was established in 2015 with the goal of "creating a drug quality programme as robust as the programmes the agency already has in place for drug safety and efficacy." Manufacturers are expected to submit ten baseline quality metrics to the FDA, with the intention of reducing the frequency of inspections for companies that (in the view of the FDA) have robust quality metrics data and therefore an implied lower risk of non-compliance. Putting aside the challenges of comparing data across different companies, or even sites within one company, there is a question as to whether compliance can be measured in this way and boiled down to a few hard metrics. Indeed, regulators are looking increasingly at a company's culture, and for evidence of its ability to self-regulate. Measuring compliance against the 'spirit of the law' requires a new set of metrics that are more risk-weighted, intangible, behavioural or intent-based.

"There has been a shift from checking that manufacturing operations are being completed correctly, to a much greater scrutiny of documentation in areas such as risk assessment, change control and deviation."

Global Head of Supply Chain Strategy

The number of FDA issued drug Good Manufacturing Practice warning letters in 2016 was 102, more than double the number in 2015 (42). The compounding pharmacy/outsourcing facility segment received more than 50 per cent of the warning letters for the third year in a row. The FDA continues to focus enforcement actions outside the US (OUS), where most generic drugs are produced.

Over three times as many warning letters were issued to OUS companies compared to domestic companies (India and China between them received 71 per cent). Warning letters citing deficiencies in data integrity remains consistent at approximately 80 per cent for OUS firms. 2016 also saw a significant increase for US warning letters citing data integrity deficiencies.⁷ Case example 2 highlights the compliance challenges faced by India's expanding pharmaceutical industry.⁸

Case example 2. Compliance challenges facing India's pharmaceutical manufacturers

Over the past decade, India has emerged as an important player in the global pharmaceutical supply chain. The country has one of the highest numbers of FDA, MHRA, and WHO-GMP approved manufacturing facilities outside of the US and Europe. However, these firms are facing a credibility crisis as they attempt to address global regulator's concerns regarding non-compliance in their manufacturing, data management and quality and control practices. Such issues of non-compliance have been penalised by large fines and import bans. Specific concerns have been cited on the credibility of laboratory tests on the quality and consistency of medicines. A Deloitte report in 2015, on the results of a survey of 33 Indian life sciences companies, pointed out that around 64 per cent of survey respondents attributed non-compliance to shortage of skilled risk and compliance staff, followed by challenges in implementing GxP guidelines (52 per cent), complying with professional association guidelines (42 per cent), and poor fraud risk management systems (36 per cent). The report provides a 'roadmap' to help develop a 360 degree compliance management system, and suggests that failure to address these shortcomings could result in business stagnation or decline.

It is a significant challenge to determine whether the end to end supply chain is compliant. With our interviewees, we explored how companies achieve visibility of compliance status across the end-to-end supply chain (from supplier to in-market distribution) and how risk is measured, processed and mitigated. While no company claimed to have a complete real-time view of compliance status across the end-to-end supply chain, some interviewees mentioned examples of portal solutions that extract data from multiple underlying enterprise systems for tracking and reporting key compliance metrics on a periodic (monthly and quarterly) basis. For these companies, however, the fact that these data are not captured on a more frequent basis or with greater granularity means that it does not represent the full picture and so does not accurately predict future compliance risks.

Supply chain complexity

Life sciences manufacturing processes, whether viewed from an internal or a supplier perspective, are often characterised by process complexity and variability. Due to the direct impact on product quality and increasing levels of regulatory inspections and scrutiny, the majority of interviewees rated manufacturing as a prime concern in terms of overall compliance risk. People, procedures and the culture of compliance were also of particular concern, indicating that the human element represents a risk to compliance for even the most stable manufacturing processes and mature quality management system. However, there is a perception that manufacturing compliance as a function is mature and well-established, and although there remains a constant compliance risk, it is for the most part well-managed and understood. Even so, the consequences of a manufacturing compliance failure can be severe (see case example 3).

Case example 3. Examples of impact of compliance failure in a life sciences company

- A) The FDA discovered manufacturing deficiencies at one major pharmaceutical company's plant, noting that some of the products did not meet testing requirements. Following a voluntary recall of these products the FDA fined the company some \$25 million for poor manufacturing practices. The resumption of manufacturing at the plant was delayed several years, and resumed only after spending over \$100 million on improvements. Although the company shifted production to other sites, a number of its products were absent from the market for several years, resulting in the loss of billions of dollars in sales.
- B) Repeated manufacturing problems caused a pharmaceutical product to contain only minimal traces of the active ingredient. The company issued a recall of the product soon after, fearing that many of the sold products were ineffective. An ensuing investigation by the FDA and Department of Justice found severe lapses in manufacturing and that recommendations and citations from five previous warning letters had been ignored. The company ended up being fined \$500 million on top of the roughly \$100 million committed to remediation activities. The value of lost sales during this process was estimated at roughly \$300 million in addition to the unevaluated loss of brand reputation.⁹

Interviewees highlighted their growing reliance on relationships with third-party business partners across the supply chain, touching on many areas that are critical to their company's success, such as R&D, manufacturing, distribution and marketing. This has increased the importance of effective third party governance and risk management. Interviewees said that compliance risks arise due to the sheer number and variety of different models, structures and standards that exist among third parties across the supply chain. These differences make it difficult for companies to get a comprehensive view of current interactions and to monitor and manage areas that could present compliance risks. In a series of reports over the past two years, Deloitte has tracked and reported how global companies are leveraging the extended enterprise also known as third party ecosystems in the pursuit of strategic advantage, and how this has created new risks arising from third party action or inaction.

“Regulators expect us to understand more about our extended supply chain, and our suppliers’ suppliers.”

Global Head of Quality

In Deloitte's 2017 report, which evaluates global companies' performance in addressing the challenges they face in managing third party governance and risk management (TPGRM), Deloitte found that while use of third-parties can help innovate and generate considerable flexibility, agility, and cost savings; any shortcomings can damage their brand and reputation, lead to regulatory penalties, and disrupt their ability to meet their customers' expectations.

More specifically, none of the life sciences industry respondents that were surveyed for the TPGRM report considered themselves fully prepared for significant change in the external environment, only 7.7 per cent of these respondents had a high level of confidence in third-party monitoring and management mechanisms and none had a high level of confidence in the technology supporting TPGRM processes.¹⁰

“For some advanced therapies such as gene editing, regulations are lagging industry, which means that life sciences companies will be judged on what they do today in 3-4 years’ time.”

Global Head of Quality

The complexity of new product types and therapies

The past few years has seen exponential growth in the development of new and more diverse life sciences product types and therapies with shorter product lifecycles. For example, the last few years has seen an increase in approvals of novel drugs, including new molecular entities and biosimilars, providing innovative treatment options for patients.¹¹ There are also new ways for assessing, approving and monitoring medical products; an increasing emphasis on outcomes; and new models for delivering healthcare, including more point-of-care testing and care delivered at or closer to home. At the same time, the pace of adoption of medical innovation is also increasing significantly (see case example 4).¹² This means that life sciences companies and regulators need to strategically reassess the implications of these new models for supply chain compliance.

Growth in the use of therapies that are a combination of medical devices, pharmaceutical therapies and digital technologies introduces a new set of previously unknown supply chain compliance challenges for both the regulator, and the company, in anticipating what the regulatory requirements might entail.

Implementing changes within existing regulatory frameworks

The management of regulatory and technical change presents a significant cost and operating challenge for life sciences supply chain companies who have to process a large volume of changes each year. These challenges are exacerbated by the introduction of continuous manufacturing and process analytical improvements, dynamic supply and manufacturing networks and expanding product portfolios. Much of the complexity involved in such change arises from the different requirements and timelines across health economies.

“All of our supply planning, quality and regulatory systems are independent systems, and coordinating between systems is a resource-intensive process involving spreadsheets as a manual work-around.”

Global Head of Supply Chain

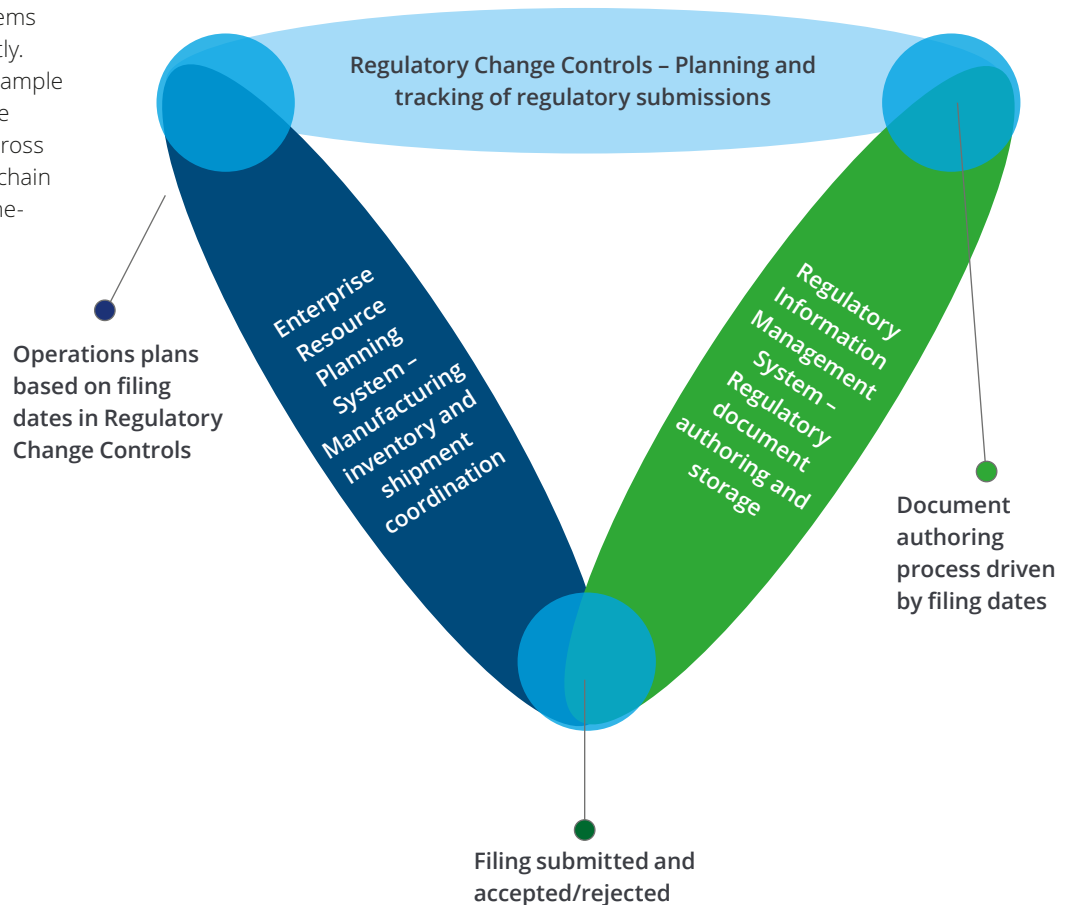
One interviewee referred to the risk of compliance gaps developing between manufacturing operations and regulatory dossiers. This may occur because process and product improvements, local market needs and safety related and other label changes need to be managed across sites and in conjunction with the regulatory dossier. Siloed enterprise resource planning (ERP), quality management and regulatory systems within a company and limited or no integration with third parties, are all making manual solutions and work-arounds prone to error, delays and exacerbating compliance risk.

Case example 4. 3D printing and its implications for the life sciences supply chain

3D Printing is expected to be worth almost \$3 billion annually by 2022. The first 3D-printed prescription drug received FDA approval in 2015. Medical devices made from 3D printing now include instruments used for surgery and devices implanted into patients. Indeed, end-use parts, such as surgical tools and device implants, are expected to become increasingly common as sophisticated metal materials for 3D printing are refined and gain approval for human contact. One challenge that will need to be addressed is whether a simpler digital workflow can be developed for creating and printing 3D objects and what this will mean for supply chain compliance.

Figure 4 illustrates the intersections between regulatory change control, regulatory information management and enterprise resource planning systems that typically operate independently. One interviewee gave a specific example of the artwork and labelling change process for which management across the regulatory, quality and supply chain functions is complex and often time-bound (see case example 5).

Figure 4. Regulatory, supply chain and document management system intersections



Case example 5. The complexity of implementing artwork and labelling changes

The regulatory function determines that a change is required and manages the details of the change that needs to be implemented, the time frames and all the associated documentation that must be completed. Supply chain and quality groups are then notified of any upcoming changes. The supply chain team, once it receives the notification, then needs to check which products are affected and start the intricate process of implementing updated packaging components as regulatory approvals are received and managing different versions of the same product to minimise write-offs and obsolescence. The quality function must then reconcile regulatory requirements to ensure that batches with the new artwork are compliant.

The increased pace of regulatory changes

Over the past few years the regulatory landscape impacting the pharmaceutical and medical devices industries has evolved significantly, shifting from local, discrete regulations to regulations with a global impact. These new regulations require regional integration and significant transformations, impacting various business processes across the lifecycle of products. Life sciences companies are realising the need to evolve and leverage synergies across various functional units – such as R&D, Manufacturing, Supply Chain, Labelling, Regulatory & Medical Affairs and pre- & post-marketing – within their organisations. Deloitte’s Centre for Regulatory Strategy has identified a number of industry and regulatory trends that companies are likely to have to respond to in 2017.¹³

Looking to the future, regulatory authorities are expected to increase their compliance oversight and enforcement activities for existing laws whilst simultaneously introducing new rules and requirements that will have a material effect on how life sciences companies do business. The capabilities of the industry have been tested by the need to interpret the legislation accurately and implement any required changes in a co-ordinated, cost efficient and timely manner across a number of business functions.

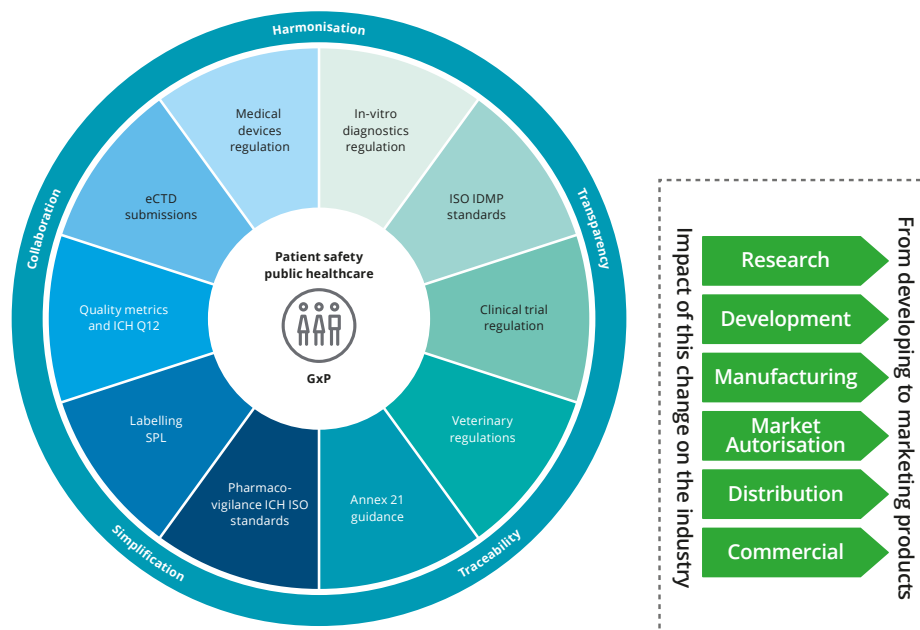
One of the most significant concerns raised by interviewees was the accelerating pace of regulatory change amid increasing complexity in the industry. Globalisation and expansion into new markets have increased the number of regulatory regimes, and the formation of new country agencies has introduced further diversity and inconsistency between regulators, placing new demands on life sciences companies. With the regulatory landscape becoming more integrated, dynamic and challenging over time, life sciences companies are having to make significant investments to achieve regulatory compliance.

“Regulators appear to lack visibility of the impact of increasing regulatory burden on life sciences companies”

Global Head of Compliance

For example, recent and ongoing regulatory changes in Europe are among the most challenging yet for the global life sciences industry, introducing a significant number of far-reaching changes across the pharmaceutical, medical devices and in-vitro diagnostics industries. Although timelines continue to fluctuate, companies will need to proactively track and monitor these legislative and industry developments, as this changing environment holds significant license-to-operate implications for pharmaceutical and medical device companies that supply products to the EU. (Figure 5 and case example 6).¹⁴

Figure 5. The European Commission’s evolving regulatory landscape impacting the pharmaceutical, medical devices and in-vitro diagnostic industries



Source: Deloitte Centre of Regulatory Excellence for Life Sciences, 2017

Case example 6. New EU regulations and regulatory changes which will impact the life sciences supply chains

A Deloitte report in March 2017 *The bigger picture: Impact of EU regulatory change on the global life sciences industry* highlights these upcoming regulations and their impact to life sciences companies. Examples relevant to the supply chain include:

- International Organisation for Standardisation (ISO) Identification of Medicinal Products (IDMP) standards – have been developed in response to a worldwide demand for internationally harmonised specifications for medicinal products. The European Medicines Agency (EMA) is taking an iterative approach to implementing the ISO IDMP standards whereby pharmaceutical companies will need to collect and ready data for electronic submission in a standardised format on an ongoing basis. The IDMP data model covers data from across the product lifecycle impacting business processes across R&D, Manufacturing, Supply Chain, pre and post marketing phases. This will require companies to make significant changes to current systems and processes, necessitating cross-functional collaboration and pave the way for transformational benefits beyond compliance¹⁵
- The new European Union Medical Devices Regulations (MDR) – aims to safeguard prompt and timely access to innovative medical devices for both patients and medical professionals and improve coordination between EU member states. Impacts include strengthened controls around traceability and transparency within the whole supply chain; increased demand on manufacturers' labelling and packing requirements.
- The International Medical Devices Forum (IMDRF) has been working with the EU and other global agencies to produce a harmonised unique device identifier (UDI) guidance, the requirements of which will be aligned with other systems such as the FDA's and those of other EU member states. Traceability includes capturing the UDI along with transactional data associated with product movement through the supply chain. Increased transparency within the whole supply chain may result in changes to supplier agreements and increased scrutiny of supply chains. Without compliance with new regulations, companies will not be able to sell and distribute products to the EU region, causing significant disruption to their supply chain network.¹⁶
- The Falsified Medicines Directive (Directive 2011/62/EU) or FMD - aims to reduce the number of falsified medicines entering the legitimate supply chain. Under FMD, all parties in the supply chain will have to make sure they have adapted their packaging lines and systems to comply with the directive by the deadline. They will also need to manage and exchange the highly complex set of product information and serialisation data with their supply chain business partners.
- Annex 21 – Importation of Medicinal Products (Annex 21 to the EU GMP guidelines) aims to address medicinal products which are manufactured in countries outside EU supply chains and imported into the EU, and the issue of multiple licenses being required if various sites are involved. Companies will need to assess whether more than one license might be needed, it is anticipated that the new guideline will provide clarity on import requirements and negate the need for double testing upon importation.
- Request for Quality Metrics: Guidance for Industry – the US Food and Drug Administration (FDA) released draft guidance for the pharmaceutical industry. This set of measures is designed to confirm that pharmaceutical manufacturers produce quality medications and drive continuous improvement throughout a product's lifecycle. This guidance's reach extends beyond the United States and will impact life sciences companies that engage contract manufacturing organisations in the processing, preparation, propagation, compounding or processing of a cover drug product or API used in the manufacturing of a drug product and contract packagers.
- The International Council for Harmonisation of Technical Requirements for Pharmaceuticals Use (ICH) – ICH Q12 – The definitions on properties and product methods for drug substances have been published in the ICH quality guidelines Q8-Q11. These guidelines describe standards for the substances' chemical, biological, and physical properties. However these guidelines do not capture the product lifecycle, particularly in regard to changes in the production process. ICH Q12 aims to fill this gap by allowing more productive and efficient management of Chemistry, Manufacturing and Controls (CMC) changes post-approval while promoting continual improvement, strengthening quality, and facilitating reliable product supply.¹⁷

While the pace and scale of existing and pending regulatory change is daunting the regulators are clear that the longer-term intention is to improve the quality and safety of products. However the exact timing of full implementation is still evolving. Once the regulatory changes are finalised and come into effect they could potentially have aggressive implementation timelines. This could cause significant short-term disruption and require large investments, in data, systems, IT and change management processes.

The challenges involved in implementing changes to existing regulations and the introduction of new ones can often be underestimated by both the industry and regulators. Some of the large and complex regulations, such as the MDR and IDMP, have been years in the making, and their sheer complexity has led to delays and changes to implementation dates. Another example of a changing implementation timetable is the California ePedigree law (see case example 7).¹⁸

Those companies taking a proactive approach to tracking and monitoring the regulatory developments and understanding their independent and combined impacts to the business are likely to be better-equipped to comply in a timely manner, differentiate themselves in the marketplace and be part of defining tomorrow's regulatory platform.

Case example 7. ePedigree law aimed at protecting consumers from contaminated medicine or counterfeit drugs

In 2004 California passed anti-counterfeiting and anti-diversion legislation, which included a requirement for an electronic pedigree to accompany drug distributions based on unique identification numbers (serialisation) affixed to each product at the point of manufacture. Due to the nature of the US supply chain, the legislation effectively meant that all products destined for the US market would need to be serialised in case they should eventually be distributed in California. The target date for implementation was 2007. The legislation created significant uncertainty and false starts for life sciences companies, and the implementation date was successively delayed until the law was eventually replaced by the US Drug Quality and Security Act (2013), with implementation dates more than ten years later than originally expected.

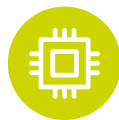
Unravelling the compliance challenge

We believe that there are actions that the industry and regulators can take to address the key challenges highlighted in Part 2 of this report. These centre on understanding the importance of culture in driving sustainable, and ultimately self-regulating, compliance and in harnessing new opportunities presented by 'big data' and analytics. This should be supported by better understanding and collaboration between industry and regulators (including regulatory harmonisation) and by the use of digital technology to improve the efficiency of supply chain compliance.

We have identified five main actions to help life science companies unravel the challenge of compliance in the supply chain:



develop an ethics driven culture, through effective leadership and governance



extract greater value from data



understand the costs and benefits of investment in supply chain compliance, talent development and/or outsourcing



build a balanced relationship with regulators, including supporting regulators to develop greater regulatory harmonisation



adopt digital technology, including robotic process automation

Develop an ethics driven culture through effective leadership and governance

Culture is a system of behaviours, values and beliefs that influence how work gets done within a company. Our previous report highlighted the importance of a culture change programme, and that companies with a mature compliance function which emphasised ethical behaviours and acting with integrity as the norm had a competitive advantage. This includes attracting high performing employees.¹⁹

“Companies need to overcome the attitude that the best way to reduce non-compliance is not to report it.”

Quality Manager

Research shows that the top five quality attributes that could serve as surrogates for evaluating a pharmaceutical company's quality culture include: a management communication that quality is everyone's responsibility; all sites having quality improvement objectives and targets; clear performance criteria for feedback and coaching; quality topics included in at least half of all-hands meetings; and regular collection of error prevention metrics. A common theme that emerged was that quality is everyone's responsibility and that providing coaching and feedback encourages employee involvement, ownership, and empowerment.²⁰

Culture needs to be embedded from the top down and actively demonstrated by the Board, with leadership's expectations made clear and cascaded throughout the company. Cultural excellence requires that all employees are passionate about eliminating mistakes by making quality their driving principle.²¹

Our previous report identified a growing movement across the industry to shift compliance programmes away from simple rules based compliance to compliance based on ethics and integrity. Furthermore, that remuneration should be linked directly to compliance with clear objectives embedded at all levels of the company; and that middle management needs to be appropriately trained and incentivised to encourage ethical behaviour in all their teams.²²

“The hardest thing is to look at something in its entirety that is fundamentally flawed and change it.”

Quality Manager

Regulators are increasingly focusing on assessing a company's culture and its inherent capability to self-regulate, over and above hard process-based metrics during inspections. For example, the FDA has proposed to formalise its assessments through a set of optional parameters that focus on quality, creating metrics in the following areas:

- a senior management engagement metric, to quantify whether senior managers who possess the means (resources and authority) to implement a change are involved with quality assessment, as well as the level of knowledge-sharing within the company
- a corrective and preventative action effectiveness metric, which highlights quality systems that rely on retraining and also provides a clear picture of the overall levels of corrective and preventative actions that a company takes.²³

The International Society for Pharmaceutical Engineering (ISPE), who has been leading efforts to bring the pharma industry and regulators together to create an open dialogue about shaping the FDA's Quality Metrics programme, has developed the Quality Culture Index.²⁴ This seeks to measure evidence of investment in building a quality culture at all levels in the company including transparent governance, whistleblowing mechanisms, incentive schemes and a focus on the measurement of prevention metrics.

Given the growing body of evidence demonstrating that a strong quality culture fosters compliance, we believe that life sciences companies should take a proactive approach to diagnosing the core values and behaviours that serve as their cultural foundation. Furthermore, they should develop a vision and roadmap that leads to a high-performing sustainable culture committed to improving compliance. Cultural change takes time to embed, which starts with identifying the critical behaviours and habits that people must commit to in order to drive the cultural vision. Systemic reinforcement comes through visible change in the behaviours of leaders and in rewards and performance management. Behavioural reinforcement requires targeted interventions that address policies and standards, operating procedures and compliance processes.

Extract greater value from data

There are clear opportunities for both life sciences companies and regulators to extract more value from data by improving IT infrastructure and systems and partnering more effectively to take an end-to-end view of the supply chain. We believe that life sciences companies could benefit from a scientific approach to data analytics to help address regulatory and compliance topics. For example, testable hypotheses can be developed that enable predictions and Key Risks Indicators (KRIs) to create insights to help look into the future to identify and quantify new or emerging risks.

Our previous report found that only 23 per cent of life sciences executives agreed that their company provided access to real-time compliance information; and only 16 per cent agreed that they had access to systems that can drill-down into key topics.²⁵ Significant opportunities therefore exist to enhance the utilisation of 'big data.' However, we do not underestimate the challenge. The evolution of many large life sciences companies, through a combination of organic growth and M&A deals, has resulted in highly complex reporting systems and platforms, each managing discrete parts of the supply chain. No life sciences company that we interviewed had a single source of 'the truth.' Even the ability to compare simple metrics such as corrective and preventative action (CAPA) across sites was problematic. Many companies are reliant to some extent on manual retrospective reporting to track or monitor end-to-end supply chain performance, including supply chain compliance.

"You need to know the guy who knows the system to get access to the data. We can't go in and get the data out."

Global Head of Quality

Although at a nascent stage in its use, 'big data' and analytics have the potential to help with the analysis of complexity. Some life sciences companies that we engaged with as part of our study are making progress in delivering compliance insights through data analytics. Leading practices that we observed include:

- increased automation and use of data analytics tools to enable better understanding of the key elements of supply chain performance
- working in partnership with data management specialists to better utilise big data sets across the supply chain, including regulatory compliance data, enabling large amounts of data to be mined to provide better regulatory reporting and transparency
- horizon scanning, enabling a forward view of regulatory updates and allowing companies to prepare their supply chains better for future changes (see case example 8).

Regulators have also identified the potential for 'big data' insights. An example is the Drug Enforcement Administration's use of mandatory controlled substances reporting to look for suspicious increases or changes in opioid drug orders, resulting in large fines for wholesalers.²⁶ Similarly, it is hoped that analysis of data collected through the Food and Drug Administration Safety and Innovation Act (FDASIA) will enable the FDA to alleviate potential drug shortages proactively and so have a positive impact on the healthcare system.

It is likely that direct data links between life sciences companies and regulators will increase in scope and sophistication. Such data links could be mined for deeper insights, as well as reducing the burden of compliance. For example, automatic data feeds from quality control (QC) checks, production performance and storage conditions might helpfully reduce the compliance burden at the time of inspection, while also giving regulators an opportunity to better understand the risks.

Case example 8. Implementation of a global compliance programme

Stringent annual process

About 10 years ago, the FDA identified a number of significant regulatory compliance issues for one leading life sciences company. This acted as a wake-up call for the company and led it to implement a comprehensive global compliance programme. By galvanising the significant localised capability across all its regions, teams across the company worked hard to understand the various regulatory requirements. This involved: stringent self-auditing, with a reliance on an extensive network of (external) auditors who do regular FDA mock-up inspections; and nearly every production or engineering function being subject to an annual mock-up audit, which is used to build next year's priorities. This builds up into a system-wide risk assessment. The company uses external auditors to help it understand the priorities and focus of regulators and how these changes over time. Given that industry regulators conduct approximately 200 inspections per year globally, these are closely monitored and responded to in a co-ordinated and managed way.

Quarterly process: product safety and compliance

Each quarter, compliance personnel conduct a 2-3 hour deep-dive on key quality processes, including supplier management, manufacturing and surveillance. This is a comprehensive bottom-up approach which provides a summary of the main findings to regional and global management. The emphasis can change, depending on findings and guidance.

Real-time processes

Day-to-day manufacturing relies on robust testing, calibration and quality assurance. The company employs a robust bottom-up mechanism of real-time reporting to identify trends spikes and variations. For example, a spike in demand for a particular spare part or component could indicate a quality issue that needs to be investigated. It also monitors closely all adverse events: defining some 80 to 90 types of events that could contribute to a potential safety incident.

Understand the costs and benefits of investment in supply chain compliance, talent development and/or outsourcing

Compliance is not generally seen as a revenue-generating business function; rather, it is a core component of managing enterprise risk and successfully executing business strategies. Due to the extent of compliance demands, many companies maintain large and growing compliance functions, incurring significant operational costs. A key challenge for many life sciences companies is that they are not able to measure, and so do not understand, the real cost of compliance. It is difficult to isolate the incremental costs of many

compliance-related activities, such as the cost of a stability test to enable a product to be launched in a new market. However, some leading companies are using their internal audit functions to undertake a critical analysis of compliance costs. The analysis is complex and imperfect, but armed with the insights they provide, companies are able to make better-informed and rational decisions that balance cost and risk and help change company behaviours.

The increasing number and complexity of regulations, talent shortages (particularly in small or emerging markets) and the constant pressure to reduce operating costs are motivating companies to consider alternative sourcing strategies. Compliance outsourcing can help companies to address compliance demands, while staying focused on their core business functions and go-to-market strategies.

Proponents argue that outsourcing frees businesses from administrative bureaucracy, while ensuring the quality, consistency and transparency needed at a corporate level to achieve compliance. Interest in outsourcing the compliance function is growing and is something that several interviewees mentioned. Compliance outsourcing providers are able to develop and maintain the necessary experience, talent, knowledge base, process frameworks, scalable infrastructure and global presence. They devote resources to monitoring and understanding regulatory demands and spread the costs of compliance across their client base. As a result, compliance needs can be addressed cost-effectively, and liberated resources can be moved to higher-value activities.²⁷

An efficient compliance outsourcing provider should deliver the following benefits:

- gains in efficiency and quality, achieved by leveraging structured processes
- access to subject matter specialists
- seamless execution of end-to-end processes, from compliance assessment through to corrective action
- flexibility to scale the deployment of skilled resources up or down as needed
- data analytics and reporting tools that provide predictive trends and insights
- reduced burden on internal infrastructure and resources
- lower costs.²⁸

Outsourcing does, however, bring its own requirements for a suitable vendor risk management programme. Such programmes should outline appropriate controls in alignment with the company's vendor management policies and associated regulatory requirements. Life science companies need to carefully weigh the risks of placing 'their right to play' with third parties.

Companies have several options when designing a supply chain compliance solution that fits their business model and corporate culture. Establishing a centralised collaborative approach to governing supply chain compliance, such as a virtual supply chain centre of excellence, can be an effective construct for a global, matrix-based company. Conversely, engaging a third party to provide supply chain compliance services can be a cost-effective model for resource-constrained companies that have limited compliance headcount or capability to implement process and technology improvements, since an outsourced model requires minimal capital investment.

Build a balanced relationship with regulators, including supporting regulators to develop greater regulatory harmonisation

As the impact of globalisation increases, with expansion of international operations and growing numbers of drug approvals, the inspection burden has become such that regulators are needing to define new approaches to regulating the industry. This is evidenced by the FDASIA initiative in 2012. Specifically, Title VII of the FDSAI allows the FDA to target its resources to higher risk facilities, with the aim of making it both more efficient and more effective in ensuring the quality and safety of drug ingredients and finished drugs. The law also provides important new enforcement tools and facilitates cooperation with trusted foreign regulators, seen as essential in a global marketplace.²⁹

“Regulators can take up to two years to report inspection results.”

Manufacturing Site Leader

Regulators increasingly work in an extended compliance environment, with companies moving into new markets and, as discussed in Part 2, increasing their dependence on outsourcing. The growing number of interfaces could mean a much bigger workload, delays in reporting results and greater risk. Guidelines may also need to be strengthened to deal with third parties, while timelines for assessment could be extended. This is a key topic that regulators should be addressing now, particularly in view of the rapid growth in outsourcing.

A data-driven risk-based approach to inspections and increasing reliance on the findings of other global regulatory partners mean that regulators can make better use of inspection capacity, reduce duplication and focus their resources on the parts of the supply chain that present the greatest risk to patient health, whether due to product quality or drug shortages.

With the move towards risk-based inspections and regulators focusing their resources more on the parts of the supply chain that present the greatest risk to patient health, there are likely to be other parts of the supply chain receiving less regulatory attention than today. In this environment, with a greater reliance on self-regulation, regulators will need to have confidence that, left to their own devices, companies will do what is right. To achieve this, the focus of regulation needs to continue its shift towards education and guidance for ensuring that companies that want to do the right thing know how to do it.

Regulators recognise the need to collaborate with the industry and to customise the support they can offer. This is particularly important in situations where new technologies and advanced therapies such as gene-editing and 3D printing fall outside existing guidance. The FDA is striving to address this by providing guidance to drug companies pursuing new technologies. An example of this is the approval in 2015 of the first ever 3D printed pill to treat epilepsy.³⁰ The FDA is taking further measures to improve drug quality and help advancements in pharmaceutical manufacturing by establishing an Emerging Technology Team, comprising representation from the Agency's Office of Pharmaceutical Quality and the Office of Regulatory Affairs – working directly with industry to help identify and resolve scientific issues for new technologies. The intention is to have early engagement to proactively identify and address potential roadblocks and eliminate potential delay in the adoption of promising new technologies.³¹

The harmonisation of regulations across the EU nations through the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA), has produced clear benefits for life science companies; in terms of supply costs, and also payers, through free movement of goods within the EU region. Regulatory harmonisation is a central tenet of the *EU Medicines Agencies Network Strategy to 2020*. Working together to improve health (see case example 9).³²

Case example 9. Collaboration and harmonisation across the EU network of national medicines authorities and with international regulators

The European regulatory system for medicines is based on a 'network' of all national medicines regulatory authorities for both human and veterinary medicines from member states in the European Union and European Economic Area, co-ordinated by the EMA and HMA. National Competent Authorities rely on each other's work to avoid duplication and share workloads and scientific competence; and member states do not conduct inspections in each other's territories, avoid duplication of assessments and work together on post-marketing safety issues.

As the world of medicines regulation has expanded globally, the need to strengthen regulatory systems worldwide has become a priority. Smaller and emerging non-EU regulators are looking to the EU network for support and capacity building and the EU model is increasingly explored as a model for other regional harmonisation initiatives. Indeed, globalisation of pharmaceutical operations has become a driver for convergence of international standards and approaches; strengthening opportunities for cooperation and mutual reliance while facilitating better use of collective resources, avoiding duplication and sharing of best practices.

The network has traditionally supported established initiatives such as the International Conferences of Harmonisation (ICH) with a view towards contributing to convergence of global standards. The emergence of new cooperative mechanisms between international regulators such as the International Coalition of Medicines Regulatory Authorities (ICMRA), the International Pharmaceutical Regulators Forum (IPRF) and the International Generic Drug Regulators Pilot (IGDRP) provides opportunities for the EU network to contribute to the future shape of international collaboration.

Collaborations are being widened further with political initiatives in the form of trade agreements between the EU and non-EU countries which increasingly include pharmaceuticals as an area of cooperation. Recent examples include agreements with Japan and Singapore. Such agreements provide opportunities to extend reliance on GMP and GCP inspections with those authorities who already apply equivalence.

“Collaboration and information sharing between regulators is increasing. Regulators can usually agree that something is wrong, but reaching a common agreement on what is acceptable is more difficult. Much more can and should be done to streamline and harmonise across regulators.”

Quality Manager

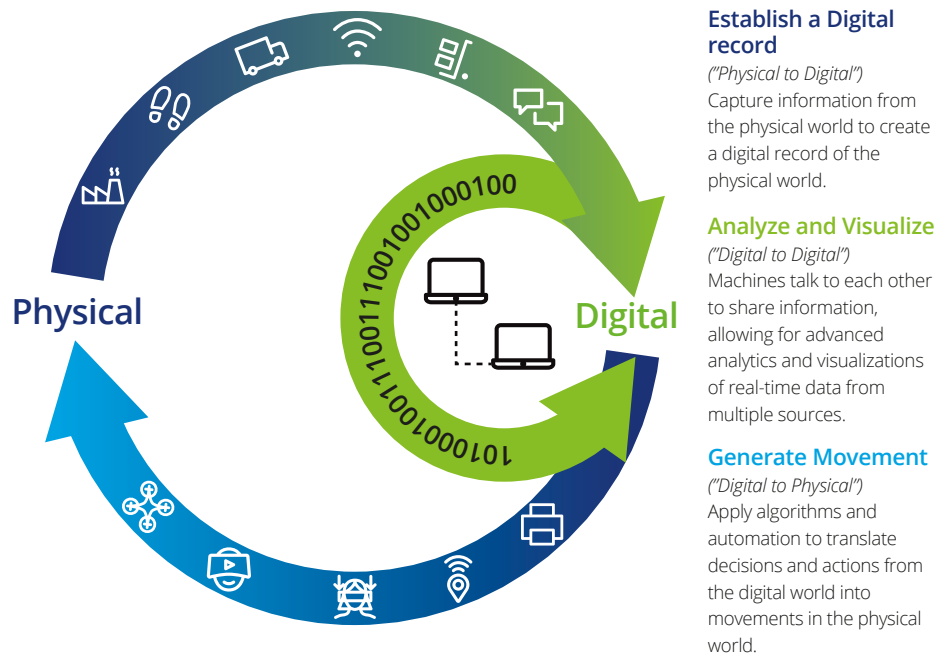
If it were possible to perform a global regulatory reset, the optimum solution for life science companies and regulators would most likely be a common global set of regulations under the stewardship of a non-partisan global regulator. In the absence of this, mutual recognition agreements between regulators (such as now exists between the FDA and EMA) are a pragmatic way to achieve many of the benefits of harmonisation without requiring exact equivalence (see case example 10).³³

While the benefits of increased harmonisation are clear, the reality is that the life sciences industry is politically important, and regulators are to a greater or lesser extent guided by the prevailing political will. In the current era, with populist concerns around global free trade and increasing protectionism, there is an emerging risk for life sciences companies that harmonisation efforts will be of a lower priority or will even retreat with the emergence of new non-tariff trade barriers.

Adopt digital technology, including robotic process automation

Digital technologies have the potential to reduce the cost of life sciences supply chain compliance and also improve its accuracy, resilience and reliability. Indeed, there is significant potential for life science companies to take advantage of the

Figure 6. Flow of information, goods and services between physical and digital worlds



Source: The rise of the digital supply network, Deloitte 2016

exponential growth of computing power, data, connectivity and new technologies to transform linear and siloed supply chain processes into what we term Digital Supply Networks (DSNs). DSNs harness the flow of information, goods and services between the physical and digital worlds (Figure 6).³⁴

DSNs provide visibility into the extended supply chain, including third party business partners and outlying operations located thousands of miles from corporate head quarter oversight. Advanced cognitive and optimisation technologies, leveraging massive volumes of data made visible through connected business partner platforms and through physical sensors and controls, have the potential to identify or even predict complex compliance challenges. For example, an increase in complaints or adverse events in multiple geographies may suggest an incidence of product tampering or counterfeiting. Concurrent supply chain planning technologies can respond immediately to a supply disturbance and identify solutions that minimise or prevent product shortages and the impact that may have on patients' lives.

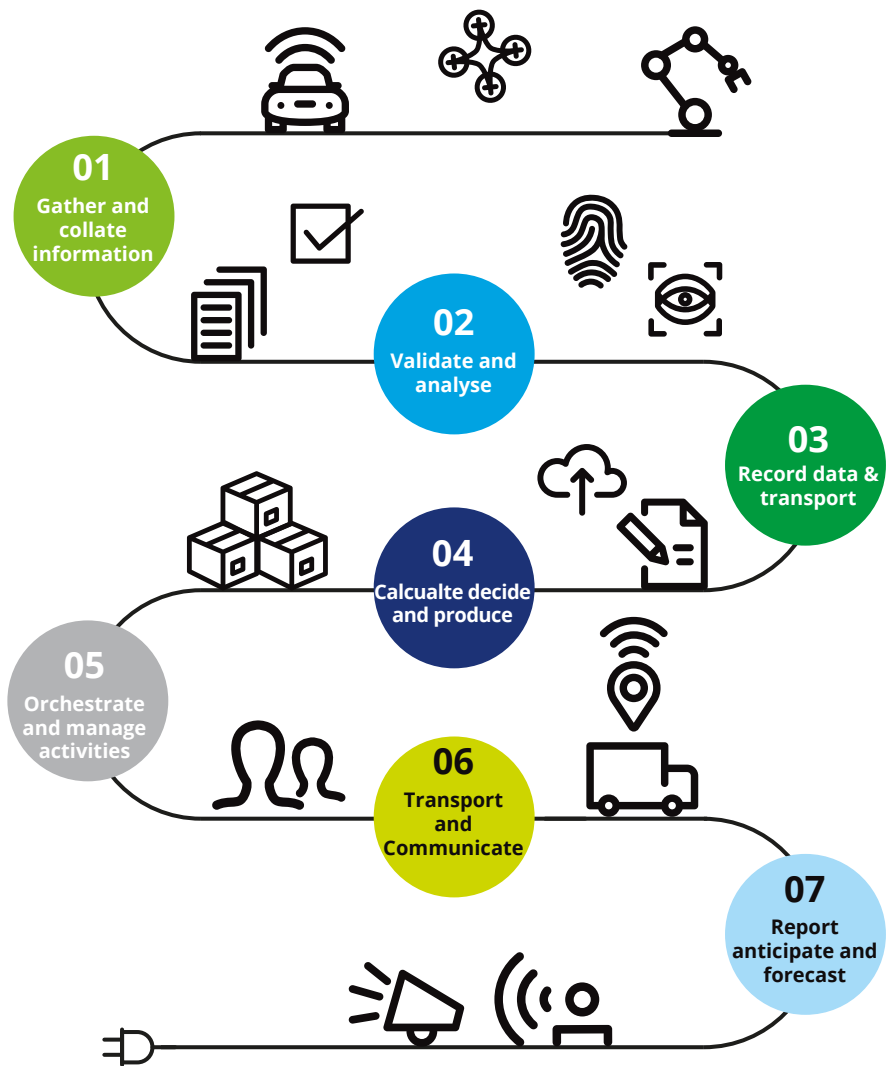
Case example 10. Regulatory harmonisation and agreement between EU and US officials on mutual reliance on each other's good manufacturing practice inspections

On 1 March 2017, EU and US officials signed an agreement, after nearly three years of negotiation, that allows the EU drug inspectors and the US FDA to rely on information from drug inspections conducted within each other's borders. Specifically, it allows drug regulators to rely on each other's good manufacturing practice inspections conducted within their respective territories, enabling the regulators to use their limited inspection resources to focus more on drug manufacturers in other countries around the world.

Many of the compliance processes required in the supply chain are routine documentation and alerts, lending them well to robotic process automation (RPA) software algorithms (robots).³⁵ Robots can operate 24/7 and are capable of capturing and interpreting multiple IT applications to enable efficient transaction processing, data manipulation and communication, providing a compelling solution to overcoming the common compliance challenges of siloed data and systems. Robots also interact with systems through existing user transactions and make decisions based on predefined logic, avoiding a need for more difficult and costly system integration. Deloitte is working with leading life sciences companies to explore the potential for robots in areas such as adverse event individual case safety report (ICSR) follow-ups and augmenting batch release processes. RPA offers improvements in productivity and accuracy for any process that is rule-based, digital and repetitive. The seven key robotic skills are shown in Figure 7.³⁶

The transition to digital technologies, while holding significant promise, presents life sciences companies with some new challenges. From a company perspective, new skills and capabilities will be required to understand and engage with all aspects of DSNs. Complexity is also likely to increase, at least initially, as digital technologies rely on a broader set of collaborations and technologies across the extended supply chain. As digital supply chains become more sophisticated, security threats increasingly become both physical and digital in nature. It is critical, therefore that a robust compliance programme includes a process for managing and monitoring cyber security threats and risks. By developing a comprehensive programme, a company can ensure that as its use of technology increases, there is a dedicated approach established to keep the company's supply chain and related data secure.

Figure 7. Seven key robotic skills to help improve efficiency of supply chain



Source: Deloitte research

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Contacts

Authors

Karen Taylor
Director, UK Centre for Health Solutions
Tel: +44 (0) 20 7007 3680
kartaylor@deloitte.co.uk

Louise Walsh
Senior Manager, Healthcare and Life Sciences
Tel: +44 (0) 20 7303 7218
lowalsh@deloitte.co.uk

John Morgan
Director, Healthcare & Life Sciences
Tel: +44 (0) 161 455 8692
jsmorgan@deloitte.co.uk

Lee Feander
Director, Healthcare and Life Sciences
Tel: +44 (0) 20 7007 2172
lfeander@deloitte.co.uk

Deloitte EMEA contacts

John Haughey
Partner, Life Sciences and Healthcare Lead, UK
Tel: +44 (0) 20 7303 7472
jhaughey@deloitte.co.uk

James Gregson
Partner, UK Life Sciences and Healthcare Consulting and Supply Chain Lead
Tel: +44 (0) 20 7007 8866
jgregson@deloitte.co.uk

Fiona Maini
Director, Life Sciences and Healthcare Risk Advisory
Tel: +44 (0) 20 7303 4767
fmaini@deloitte.co.uk

Hanno Ronte
Partner, Life Sciences and Healthcare Monitor Deloitte
Tel: +44 (0) 20 7007 2540
hronte@deloitte.co.uk

Tom Van Wesemael
Partner, Life Sciences and Healthcare Global Supply Chain Lead
Tel: +32 499 5 73 25
tvanwesemael@deloitte.com

James Wright
Partner, Life Sciences and Healthcare Tax
Tel: +44 (0) 20 7007 3979
jnwright@deloitte.co.uk

David Hodgson
Partner, Life Sciences and Healthcare Risk Advisory
+44 (0) 20 7007 9934
davhodgson@deloitte.co.uk

Deloitte project team

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Fax: +44 (0) 20 7583 1198.

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