BEYOND MANUFACTURING: INDUSTRIALISATION OF DRUG DELIVERY IN THE REAL WORLD

When discussing the industrialisation of drug delivery, it is natural to focus on the processes and management of manufacture. Here, Napoleon Monroe, Managing Director, New Directions Technology Consulting, provides a different perspective on the idea of drug delivery's "Industrialisation" and what that might mean in the modern world of service industry.

The industrialisation of drug delivery extends well beyond the research lab and production facility. Healthcare, including pharma in the US and elsewhere, is being driven by forces, developments and complexities beyond the control of the legacy stakeholders. This article provides an overview of a wave of industrialisation sweeping over the pharma sector. Some aspects of these changes present opportunities, some are highly problematic. The observations discussed herein may relate as well to research and pharma manufacturing, however, while wide-ranging, this article is not all-inclusive.

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THE DRUG DELIVERY INDUSTRY

Drug delivery is already an industry, albeit a fragmented one, with many stakeholders (see Box 1). It is an industry that often takes on different forms between one situation and the next. For example, drug delivery is not the same industry as it was just a few years ago when the manufacturers' supply chain essentially ended with a product being delivered to another company. Now in drug delivery, the patient is commonly regarded as the end-point. Drug delivery is changing to include lessons, realities, techniques and concerns from other industries. The industrialisation of drug delivery has brought progress but, in some ways, there is still more promise than progress. Like it or not change has, and will continue to, come. The challenge is: How do we humanise industrialisation to better benefit patients, other stakeholders and society?

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PRACTITIONERS AND HEALTHCARE SYSTEMS

Many years ago, doctors compounded and delivered patient-specific medications themselves on a case-by-case basis, with far fewer products, none biotech, to consider. Injections, except insulin, were given in the office. This is simply no longer the case.

Many practitioners express a preference for the "good ol' days" when their decisions were not challenged by the new norms and complexities inherent to the modern healthcare industry. When they did not have to rely on staff, managers and computers to practise medicine. When they could give a low-income patient, who could not afford an autoinjector, a syringe and a vial of epinephrine without fear. They wish they did not have to waste time on badly designed medication reconciliations in electronic medical records (EMRs) and complex billing codes. There were few expectations for service and support for patients until the next office visit or house call.

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Pharma's customers were the MD decision-makers in individual practices. Until rather recently, practitioners relied on approvals from clinical trial data and what pharma representatives told them.

Nowadays, patient centricity has become a healthcare mantra. Professional specialisation and drug delivery by non-MDs, including patients themselves, have changed drug delivery and disposal requirements. Healthcare organisations track re-admissions and follow cases into the real world over time. Healthcare mergers and acquisitions both within and outside pharma have changed the decision-making process for drugs and drug delivery. Product performance evaluations are becoming part of healthcare provider and payer value models. Purchasing decisions are more made by non-MD general and materials management professionals and are based on proven relative product value. Payment for outcomes is becoming a reality. Pharmacy benefit managers and other stakeholders have inserted themselves into the decision and reimbursement processes.

Practitioners and staff now often work for corporations. Clinicians are overwhelmed with raw data, which is not parsed into useful information. Professional interactions are timed, as are the activities of production line workers. Models from other industries such as the checklists used in aviation and the Toyota Production System are now part of healthcare best practices.[1,2]

CONSUMERS, AKA PATIENTS

Until somewhat recently, patients were relatively uninformed about the drugs that they were prescribed. For most insured patients, drug costs were not a significant factor. However, patients are now required to pay a greater share of their pharma expense. This drives a greater desire for pharma information, leading to the situation now where pharma has to increasingly deal with patient/payers who have come to expect instant gratification of their desire for product information.

The big tech companies, such as Amazon, Apple and Google, "get" these consumer desires, building success off the desire for instant information. Amazon's subscription model, one-click ordering, preferred product selections, verified purchase reviews, personal order history and "customers also bought" features; Apple's Genius Bar; and Google's assisted intelligence have changed the retail, publishing and search industries.

BOX 1: STAKEHOLDERS IN THE COMPLEX DRUG DELIVERY INDUSTRY

- Patients
- Payers (patients (again), taxpayers (again), government entities, true insurers (patients, National Health, Veterans Administration, Medicare, Medicaid, employer plan sponsors), some other insurers (companies that mainly administrate and negotiate, only paying after certain conditions have been fulfilled, e.g. after plan limits have been reached)
- Regulators
- Legislators and voters
- Pharma manufacturers and their CROs, CMOs, API and excipient suppliers, and venture partners
- Stockholders and financiers
- Insurance administrators and brokers
- Combination products manufacturers and their component manufacturers and processors
- Medical practitioners including pharmacists
- Distributors and marketers, including wholesale, retail and pharmacy benefit managers (PBMs).
- Consultants, lobbyists, media, publishing and advertising interests
- Politicians, especially legislators and governmental officials
- Patient advocacy groups
- Professional and trade associations
- Standards development organisations
- Data carriers, analysts and aggregators
- Academics
- Litigators
- Others

NOTE: Employers, employees, families, caregivers, contractors, lobbyists, consultants and even friends of all of the above. Interrelationships and ranking of importance change situationally issue-by-issue.

These companies and others assist their customers and use their informatic tools to extend the functionalities of their supply chains to end-users and other stakeholders.

Patient and caregiver reliance on internet-based information for most products is not as restricted as it is for pharmaceuticals, however. While the US allows direct-to-consumer advertising, there are still restrictions on what can be said in internet-based information. Patients, however, can increasingly say what they want, leading to the idea of "ask your doctor" being supplemented by "voices of patients" online. As with other social media, these voices are changing the amount and content of drug delivery information and influencing a change in drug delivery models. Stakeholders are coming to rely more on patient input well beyond the clinical trial.

CHANGES FOR OTHER STAKEHOLDERS

The pharma product mix and consolidations at pharma-related companies have changed drug delivery. Specialty pharma products are usually expensive and require more care and supporting information. Many are injectable and are delivered outside institutional settings. Specialty pharma, especially biotech, has become the leading revenue source for the pharma sector, with the age of the "blockbuster" drug product clearly waning. Products of the much touted "personalised pharma" concept follow the specialty pharma model.

Consolidations in and around drug delivery provide economies of scale and enable the adoption of technologies developed in other industries. Specialisation around diseases and mergers, such as that of Express Scripts and the insurer Cigna, are examples of growing scale and cross-industry consolidation. Some pharma stakeholders have been reluctant to adjust to some of these changing industrial realities.

ADVANCES IN DIGITISATION

Consumer retail long ago adopted the EAN/UPC barcode in advance of any governmental requirements. Only since 2013 have drugs and medical devices seen the introduction of standardised automated identity and data capture systems (AIDC), including barcoding and serialisation, for pharmaceuticals, devices and combination

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products. The US Drug Supply Chain Security Act (DSCSA) and the Unique Device Identifier (UDI) regulations were largely proposed in response to the desire to rid the supply chain of unapproved, counterfeit, illegally diverted and recalled products.

Beyond these objectives, AIDC gives healthcare a language for gathering other information and allows automation of information collection. The common language feeds "big data", allows for aggregation, facilitates analysis and can bring greater transparency.

Financial information, such as pricing, is not part of the US DSCSA and UDI. However, standard nomenclatures, as seen in databases related to these programmes, can be used as a means for gathering financial information. Pan European Public Procurement Online (PEPPOL) is used in some UK trusts and elsewhere to gather pricing and other information beyond the scope of the US regulations. Some non-governmental organisations (NGOs), including some for-profit organisations, are also aggregating information beyond the regulatory requirements. Healthcare specialities are moving toward standard diagnosis, treatment and adverse effect codes across professions.[3] In the US, even in the absence of a national health system, stakeholders are pushing toward EMR interoperability.[4]

AUTOMATION AND TELECOMMUNICATIONS

There are now internet-connected refrigerators, doorbells, toothbrushes and many other such connected "things". It should be no surprise then that automation and telecommunications continue to penetrate healthcare and, specifically, drug delivery. For example, automated "robo-call" medication refill reminders are commonplace. Connected autoinjectors are on the market and, with a new strap, an Apple Watch can be made into an electrocardiogram (ECG/EKG).[5] Standards are in place for regulatory-compliant data transmission.

As in other industries, the range and number of internet-connected healthcare "things" continues to grow, adapting applications, sensor, power and analytical means from other industries. Because of the importance of pharma regimen compliance, vital signs monitoring and the human factors which can impact drug delivery, these connected healthcare "things" are more useful in meeting real needs than some connected "things" in other industries.

DISRUPTION

Retail booksellers were quite complacent when Amazon first began selling books in 1995. Drug delivery companies are now trying to avoid a similar disruption, with new entrants and combinations in drug delivery worrying legacy stakeholders. Examples abound:

1) Amazon buys PillPack and introduces an over-the-counter pharma line.
2) CVS buys Aetna.
3) Apple re-enters healthcare with Apple Health.
4) Berkshire, Amazon and JP Morgan appoint Dr Atul Gawande as CEO of their newly formed healthcare company.

Publicly listed pharmacy companies took a hit to their stock on the day Amazon announced the PillPack purchase. Combinations are one response by legacy companies.

DEPENDENCIES FOR SERVICES AND DEVICES BEYOND MANUFACTURING

Years ago, there was little demand for "service beyond the pill" and little pharma interest in supplying it. Most pharma companies were not traditionally very engaged in home-use delivery systems beyond oral solids and liquids, topicals and sprays. Indeed, pharma still often relies on contractors to design and manufacture delivery devices. These devices and their component providers are often offshore and rely on standards such as ISO 13485.

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Pharma relies on pharmacists and others to assist with providing service. Pharmacists have been expanding their roles since the beginning of the generic movement. Beginning with the biotech revolution, pharmacy benefit managers and specialty pharmacies are coming to have larger roles.

Pharma, practitioners and patients are somewhat co-dependent in reporting medical effects, behaviours and compliance with the pharma regimen. Contract outsourcing and assisting patients have added layers of responsibility to the pharma industry. Devices and services from non-pharma companies have become part of a landscape of the drug delivery industry, thereby further pushing the drug delivery industry past just research and manufacture towards being a fully-fledged globalised service industry.

The relatively new (2002), US FDA Office of Combination Products works to bridge the regulatory gaps between pharma, software and device industries. These industries, and human factors professionals, are industrialising drug delivery supply chains to extend to the patient wherever and whomever they may be.

INTERNATIONAL STANDARDS AND REGULATORS

US companies have often lagged behind in the standards-setting process. In the US, ISO and other international standards were, and largely still are, "voluntary". The reality is that more regulators, and other stakeholders, in the US and elsewhere are relying on international standards. Such, increasing reliance impacts timing for regulatory approvals, cost, litigation defence, marketing plans and return on investment (ROI).

Quality systems audits that help ensure that planes don't fall from the sky because of component or systems failures are already in place in the aircraft industry. Aircraft parts are customarily serialised, tracked and traced. The Aviation Suppliers Association, working with the International Accreditation Forum (IAF), helps manage

such a system for the aircraft and other industries. Some industries have agreed to audit databases so that stakeholders can rely on audit certificates.

Neither drug delivery companies nor their regulators can effectively audit the quality systems of everyone supplying components and finished products into the US. The IAF has proposed a registry system for valid ISO 13485, the Medical Device Quality Standard. Also, some regulators are working to implement a new Medical Device Single Audit Program (MDSAP).

ABOUT THE AUTHOR

Napoleon Monroe, Managing Director of New Directions Technology Consulting, has a diversified background that extends from developing and producing emergency pharmaceutical delivery systems to managing private brands for a Fortune 500 company, to building and managing the IP portfolio for a company that is now part of Pfizer. His expertise includes product development, licensing, regulatory processes as business opportunities, risk management and international marketing, with experience managing business relationships in more than 30 countries. Mr Monroe has led teams that have invented and commercialised major products, such as EpiPen and ATNAA.

Success in randomised clinical trials is being augmented, even supplanted, by real world evidence. Regulators' drug adverse event and medical device reporting systems are being supplemented by the FDA's National Evaluation System for (medical) Technology (NEST), which can trawl the internet to capture patient experiences.

THE REALPOLITIK SURROUNDING PHARMA AND DRUG DELIVERY

Legislative and regulatory discussions surrounding drugs and drug delivery are loud and fractious. Ethical lapses and erroneous assumptions highlighted by the media pose a high risk of generating anger among stakeholders. The pharma pricing model in the US was, and still is, quite opaque. Legislative and regulatory pressure on rebate systems and pricing is building. Globalisation continues to be a factor, especially in multinational pharma companies.

While there are economies of scale for regulatory harmonisation, regulatory nationalism is now more of a factor, for example China has a different standard for barcodes and country-specific symbol and language requirements seem to be becoming more prevalent. With an eye on digitisation, data ownership and security are issues for real world data collection, with various governments introducing or looking to introduce new, stronger data laws, such as the EU's General Date Protection Regulation (GDPR).

SUMMARY

The factors discussed in this article have changed other industries. The drug delivery, pharma and related stakeholder industries are engaged in change management exercises. The magnitude of what they are trying to manage can be seen when one examines changes wrought in other industries. To quote Sam Cooke:

"…I know a change gonna come…"

This article reflects the author's personal opinions and analysis. It is not a professional interpretation of any medical, regulatory or legal requirements. The author, the licensees to his intellectual property and his clients have interests in healthcare with a focus on medication telemanagement.

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