ACCELERATING THE ADOPTION OF CONNECTED COMBINATION PRODUCTS: PATIENTS, MANUFACTURERS & PRACTITIONERS CAN LEAD

In this article, Napoleon Monroe, Managing Director, New Directions Technology Consulting, asks why connectivity has failed to advance rapidly, and argues that many stakeholders can benefit if the adoption of connectivity for drug delivery can be accelerated. While this article will centre on pharmaceutical combination products, the essential points also relate more broadly to pharmaceuticals and medical devices.

As discussed in "*Combination Products Can Benefit Most from Serialisation*", our October 31, 2017, PDA Letter article, "Four years after the rulemaking and legislation for standardised automatic identification and data capture (AIDC) requirements for prescription pharmaceuticals and medical devices, scanning is minimal."

Now, six years down the line, this still holds true, scanning is still minimal. Yet enablers for connectivity are in place: device-connected smartphone apps, open APIs regulated by FHIR are known, standardised AIDC including serialisation for the US prescription pharmaceuticals is bound by law, investments in the Internet of Healthcare Things (IoHTs) including remote diagnostic devices have been made, cloud-based big data processing capability is real, and well-developed security systems including blockchain technologies are part of supply and information chains.

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Accelerators for connectivity abound: the biotech revolution necessitating patient-used combination products (wearables, implantables, pens, inhalers, autoinjectors, kits) has redefined the point of care to be "wherever the patient is"; regulators are fast-tracking approval; compliance problems and related costs are well publicised; regulators demand real-world evidence; drug price reduction pressures are in the press daily and payers ask for payment-for-outcome programmes; pharma and other stakeholder consolidations provide economies of scale; and disruptors are fundamentally changing healthcare and pharma market structures.

Nonetheless, the tenor of the healthcare connectivity discussions, especially at the most recent conferences, has convinced me that the approach of everyone trying to connect everything in healthcare will continue to fail.

There must be a far better way to start somewhere and implement meaningful connectivity, especially for expensive, fragile combination products in patients' hands. A focus on achievable goals would be more beneficial.

Connecting combination products in the US healthcare systems can be achieved by manufacturers supporting their prescribers and patients. Patients who are prescribed combination products have diseases which are expensive to treat. Capturing

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information on combination products is useful and societally beneficial in the short and longer term.

The global healthcare industry and governments have spent billions of dollars on manufacturing, tracking and regulating pharma and medical devices; and on highly unpopular electronic medical records / electronic healthcare records (EMRs/EHRs). Healthcare manufacturers and distributors have spent millions on placing barcodes, including serialised barcodes, on their prescription products and on devising software to report the data. Yet, thus far, practitioner scanning product bar codes into EMRs and fully integrated supply-chain use by manufacturers and distributors are exceptions, not the accepted best practice standards, meaning that the returns on all these investments are miniscule.

At conference after conference, practitioners, pharmacy benefit managers (PBMs), pharmacies, manufacturers, distributors, patients and patient advocates, industry, taxpayers and their advocates, plan sponsors, regulators, payers, lawyers, lobbyists and other experts bemoan the fact that none of these investments have yielded meaningful improvement in outcomes. And all the while, self-evidently, everyone wants better patient outcomes.

EVERYONE WANTS BETTER PATIENT OUTCOMES

Patients most especially, need help to improve their outcomes. Patients and the combination product manufacturer have the greatest combined financial and outcome interests in the information about the treatment.

The real world is now full of consumer healthcare recording tools, connected medical devices, patient portals, journals and logs, environmental monitors and connected combination products. Consumer behaviour is becoming better recorded, analysed and understood from their combination products, medical devices, consumer devices patient medical records. Every patient is different to some extent.

Patient ownership of their EMR information is finally being promoted in the US by federal policies. But the patient cannot easily aggregate their own data, nor may they understand it fully. Patient data is a major revenue source for the aggregators, but patients are becoming ever more wary of the use of their data.

Practitioners (prescribers), nurse practitioners and physicians' assistants are usually not pharmacists. Patients have multiple prescribers. Patient memory and knowledge is faulty. Compliance is known to be terrible. "Patients lie about the taking of medications", is a rough translation from Hippocrates. Patients forget, they have little experience with medication, and little knowledge of brand and generic names and dosage strengths. This often makes medication reconciliations, when the prescriber asks, "Has anything changed with your meds?", a pointless exercise. Even a review of a previous list of medications for updates is often a waste of time. While practitioners may want to be able to help patients and help limit patient costs, payments to practitioners for drug follow-up are poor.

Clearly, any data captured in a manufacturer-sponsored program should be transferred to the practitioner and the patient's record. Trust in pharma is such that pharma manufacturers may wish to train and reimburse provider call-centre pharmacists.

Pharma manufacturers' profitability is largely tied to specialty drugs, often combination products. Manufacturers want patient and prescriber loyalty, better control of their products, and means to prove and improve the value of products. In many countries, pharma manufacturers have lost much of the control of pricing to the numerous intermediaries that have (in different ways in different countries) structured opaque pricing schemes outside of pharma's control. Pharma manufacturers, while not blameless, get more than their fair share of the blame for price increases.

Direct pharma to patient communication is usually limited (in the US) to non-targeted DTC advertisements and practitioner office media. In other countries there is no such direct contact at all. Patient communication should be available to practitioners and pharma as well as to the patients and their designated caregivers. Data sharing could, and arguably should, be limited to the manufacturer, the prescriber and the patient and their approved persons.

Manufacturers and their distributors want to secure returns on their investments in products and AIDC.

Combination products are used outside institutions and are therefore subject to myriad human factors issues. Adding connectivity and professional advice can help address the human factors questions. Connectivity allows practitioners and manufacturers to understand the outliers.

Patient package inserts are generally not read. Even if they attempt to read them, the inserts are not understood by the average patient. Patient website searching gives general information which may or may not be applicable to the patient. Manufacturers can assist the practice of medicine and pharmacy by providing truthful professional advice. Such professional advice is not regulated in most countries (e.g. it's not regulated by the FDA in the US). Pharma has an interest in having patient information quickly. Preferably in near real time. This can enable information and assistance to be provided before an adverse event or before someone unknowledgeable misinterprets patient information and starts making erroneous assumptions. Professional intervention through connectivity could allow the pharma company to provide great value while not having to address every regulatory "What if….?"

Pharma is already being asked to assume payment risk in outcomes-based payment plans. Is connectivity costly? Yes, but not so costly as the inability to manage the business. One of the largest manufacturers repeatedly asks me "where is the value in connectivity?" That company just began offshore trials of connectivity.

Connectivity does add cost and complexity to already complex, costly and profitable, combination products. Connectivity also allows manufacturers to avoid the hidden costs of existing system complexities.

Regulators want to improve product safety and efficacy and there is pressure on them to approve new treatments rapidly. Behavioural and social variables are factors in adherence and, in this regard,

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regulators have realised that the prospective approaches of randomised clinical trials are inadequate. In particular, they often do not fully capture information on subsets of populations, which relate to age, ethnicity, sex, co-morbidities, genetic variations, and other factors. This, and other limitations of randomised clinical trials, and also their high costs, are moving regulators toward demanding that stakeholders collect and analyse observational real-world data to build real-world evidence for safety and efficacy. The great unstudied subset is those patients whose social circumstances or behaviours are unusual. There is a clear case for adopting connectivity as soon as possible to get the most favourable outcomes from approved combination products.

Payers want to limit costs. And in the same way that regulators are getting behind real-world data, the trend with regard to payers is also toward building real-world evidence for comparative cost effectiveness. If the manufacturer of a combination product cannot prove their case, the manufacturer of that combination product will suffer. Or, looking at it the other way around, if one manufacturer can demonstrate their product's cost-effectiveness unequivocally by using real-world data, and another cannot, the manufacturer who can is at a distinct advantage. These are realities even before the announced programmes from the US Department of Defense, Veterans' Affairs and EU's Pan-European Public Procurement Online (PEPPOL) initiatives I discussed in my previous ONdrugDelivery articles (see bibliography) take full effect.

Retail pharmacists, PBMs, pharmacy technicians and sales clerks are not diagnosticians. Often the patient-pharmacy interaction is perfunctory: "Do you have any questions today? Next customer please." Home health visits by nurses and pharmacists can be helpful but are just snapshots, not ongoing views, of the patient or of medication performance. Such visits do not update for adverse reactions or lifestyle changes between visits.

Insurers for commercial employee plans are largely processors for plan sponsors. Provider payer insurers are true insurers. Insurers for commercial employee plans are not driven primarily by the patient's needs nor by the patient history. They do not prescribe, but can limit access to certain drugs and can disintermediate other stakeholders from the decision process.

EMR/EHR Companies' products might function well in theory but in practice the data inputted is often incomplete, out of date, inaccurate, inaccessible across providers and to patients, and far from interoperable across multiple providers and pharmacies. The products are not designed to interpret important evidence, and the data is often only accessed at the time of healthcare practitioner (HCP)-patient interaction.

Many EMRs were built primarily to manage payment and, as reported in a March 2019 Fortune Magazine article, are viewed by practitioners as *"Death by a Thousand Clicks"*. EMRs contain professional information and are not integrated with personal health records. 99% of daily life for the non-hospitalised patient takes place *in between* their interactions with HCPs but EMRs don't log this or reflect it in any meaningful way. Immediacy of information capture is often essential. Memories fail. You can't write it all down. Yet complete, meaningful medication histories and reconciliations, and an understanding of symptoms and behavioural variables would be valuable to all stakeholders. Connected devices, especially connected combination products, can help deliver this.

Legislators are under political pressure to reduce the total cost of pharmaceuticals, which is building rapidly. And some of the regulatory changes which would enable and incentivise connectivity require legislation. Legislators want to help constituents, they also want to be re-elected. These are sometimes mutually exclusive. The US legislative process is currently at a virtual standstill, lawsuits abound, the cost to achieve legislative resolution will be high, the wait long, and the outcomes uncertain.

Many Other Stakeholders have their own interests. Even not-for-profit entities have financial imperatives and desires to expand. Stakeholders are not monolithic. There are silos of interest within each.

QUESTIONS AND CONCLUSIONS

We are at an inflection point. Expensive specialty products are key to improved health, pharma profitability and healthcare cost containment, and all stakeholders naturally want their own needs to be met. Yet the complexities of the healthcare marketplace and of healthcare information systems boggle the mind. It seems everyone is collecting data but few are able extract and interpret meaningful evidence. Medical records and prescription medical products are becoming like banking records. Your chequebook and each cheque in it are serialised and prescription drug products are as well.

Connected systems offer a route toward making sense of the real world situation and a route to meeting the needs of many stakeholders. Questions of who has the most to gain or lose from connected systems may determine outcomes for the future of connected healthcare, and the words healthcare systems overall:

Q. Which stakeholder really has the true patient relationship?
A. Arguably, in our current reality, no one.
Q. Who has the most at stake in each patient situation?
A. The patient.
Q. Who knows the most about a given drug?
A. The pharma manufacturer.
Q. Who knows or should know the most about each individual patient, their activities and related human factors?
A. Prescribing doctors.
Q. How can the data received, especially from patients, be validated, secured, understood and used to improve patient and population health?
A. By pharmacists who are knowledgeable about the drug and the patient receiving and interpreting the data for the patient and the pharma company.

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can be effective in promoting compliance and improved outcomes and lowering cost. Meddling by unknown, unknowing, uninformed data collectors cannot.

One can envisage a new paradigm with software proprietary to pharma (or other) companies, shared with the informed approval of the patient at the time treatment begins and as necessary with prescribing practitioners first and others as treatment progresses. Obviously, the patient and other stakeholders must be assured that their information is secure. An example of a company developing sophisticated security and privacy platforms which could enable this focused data sharing, and linking it with identity proofing and transparency to the blockchain, is WebShield (San Francisco, CA, US).

As discussed in my June 2019 ONdrugDelivery article, *"Connectivity Restoring Trust in Pharma Communications"*, much trust in pharma has been lost. Becoming more patient centric and better supporting and, within ethical limits, controlling, their products can allow pharma to build trust. Pharma will be well served if it seizes the opportunities presented by connectivity and applies connectivity in its specialty and combination products to make outcomes better.

Transformational medicine requires a focus on achievable goals. In the US healthcare system, and in an increasing number of healthcare systems further afield, connecting specialty and combination products has become an achievable goal, and it can be transformational. Pharma, along with practitioners and patients can lead in the transformation.

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