Capgemini Consulting

DIGITAL LEADERSHIP

An interview with

Bernard Vrijens

Chief Science Officer, MWV Healthcare

Transform to the power of digital

Bernard Vrijens, PhD
Chief Science Officer
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Introduction

MeadWestvaco (MWV) is a global packaging company with products in various consumer markets including healthcare, beauty and personal care, food and beverage, and home and garden. Operating for over 150 years, MWV has 15,000 employees worldwide and facilities in 30 countries.

MWV Healthcare has created leading-edge digital packaging solutions designed to measure and improve patient adherence to courses of therapy. A study realized in 2012 by Capgemini Consulting and Healthprize Technologies has estimated the cost of non-adherence to the pharmaceutical industry globally as $564 billion every year, thus making it a major improvement opportunity for the industry.

Capgemini Consulting has interviewed Bernard Vrijens, PhD, Chief Science Officer for MWV Healthcare. Dr. Vrijens was General Manager of the AARDEX Group, prior to AARDEX becoming part of MWV Healthcare in 2012. In this interview, he shares his views on how digital technologies can help improve patient adherence.

Capgemini Consulting: In your opinion, what are the greatest challenges of the current drug development process?

Bernard Vrijens: With increasing complexities including less tolerance for risk, rigorous regulations, elongated timelines and growing costs, it has never been more difficult, expensive or time consuming to develop safe, effective medications. Nevertheless, over the last four years the number of registered clinical trials has more than doubled[i], and as of March 2014 there were over 160,000 trials registered with the Food and Drug Administration (FDA),[i] creating an even greater need for improved efficiencies across drug development.

These changes put a premium on accurate results and that, in turn, make it even more important to assure that patients are adherent to their medications – taking them in the proper amount, on time, and in the right way. Yet patient adherence is inconsistent – and has been that way for decades. For chronic illnesses, studies show that as many as 50 percent of patients are substantially non-adherent.

> *"It has never been more difficult, expensive or time consuming to develop safe, effective medications."*

Non-adherence is a serious challenge, in both routine medical practice and drug trials. But the implication of non-adherence in clinical trials is far greater than just one individual, since each trial patient contributes to the body of data that determines the safety and efficacy of the medication.

Patients in clinical trials skip doses, stop taking their medications and misunderstand instructions. And they don't always tell the trial staff – either because they want to please the study team or are concerned about being dropped from the study. The fact is we're all human. We're imperfect, we make mistakes, we forget. When trial organizers have a better understanding of what's actually happening among the treated patients, they can guide intervention aimed at achieving and maintaining good adherence.

Capgemini Consulting: : If non-adherence is an issue in product development, can you explain how it works in real life?

Bernard Vrijens: So, when we talk about patient non-adherence, we make the distinction between three elements: initiation of treatment (when the patient gets the prescription, and if/when the patient starts treatment), treatment implementation (which means the medication is taken as prescribed, for example – taking a dose once or twice a day, with or without food, etc.), and lastly, if/when the patient discontinues the treatment, with or without instructions to do so from the prescriber. The most expensive drug is the one that is paid for but never taken.

Initiation is a major issue in the practice of medicine, but not so much in product development, because patients are selected to participate in a trial, and usually have a higher level of motivation. Both financial incentives and an established relationship with a healthcare provider are usually involved.

However, the implementation and discontinuation pieces are an issue, whether you are developing a new medication or prescribing a marketed medication to a patient for ongoing care. Even in clinical development, patients go back to their daily habits (e.g., going out on weekends and missing the Friday evening dose, forgetfulness). We know that patients' reasons for non-adherence are largely behavioral, so we must create interventions and solutions that address patient behavior and help them create an "adherence habit."

[i] Clinicaltrial.gov

> *"The most expensive drug is the one that is paid for but never taken."*

Capgemini Consulting: So, how can digital solutions help address the issue of non-adherence?

Measuring adherence is critical in the drug development process, particularly during the treatment implementation phase. Digitally detecting when a patient accesses his drug package is a good estimate of patient adherence. Studies have shown that when a patient accesses his or her medication package, there is an extremely high likelihood that the drug will be administered. In fact we have found less than 2 percent discrepancy between opening the package and swallowing the pill in the case of orally administered drugs.

> *"Digitally detecting when a patient accesses his drug package is a good estimate of patient adherence."*

Knowing this, we can use smart digital medication packaging as an easily implemented tool with low safety barriers to monitor patient adherence and drug exposure during clinical trials.

Digital capabilities allow us to automatically compile important data from the patient that are valuable for both the trial organizers and the patient. Such data can be used in a number of ways. (1) You can adjust the trial data analysis and have valid estimates of what truly happens in the clinical study, in some cases in real time. (2) You can share information with the patient about his/her adherence patterns in real-time, which has been shown to positively change his/her habits - sometimes quite drastically. MWV Healthcare is currently involved in a Hepatitis C development study where we are reaching a very high level of patient adherence when we provide factual feedback on recent dosing history to the patient – objective evidence on how well or poorly the patient has been adhering to the prescribed dosing regimen. (3) You can use these data to select the most adherent patients for special studies. These strategies have been recently recommended by the FDA in its draft guidance on trial enrichment strategies. (4) You can show the full efficacy of a drug before moving on to testing it in broader populations. So by selecting patients with the highest level of adherence one gets closer to a reliable analysis regarding the full effects of taking the drug according to the prescribed dosing regimen. Data from partially adherent patients can show the consequences of various deviations from the prescribed dosing regimen. Such data may lead clinical researchers to revise the recommended dosing regimen, if, for example, the data show superior results from taking lower or less-frequently administered drug than called for by the original dosing instructions.

> *"Efficacy is defined as the full therapeutic effect of a treatment when it has been taken as prescribed."*

Capgemini Consulting: Considering how impactful digital solutions can be for drug development, help us understand what solutions are out there?

There is good evidence that informing patients in real-time about their recent dosing histories with the various drugs they are prescribed has a strong effect in improving their adherence. Simply showing patients how they're taking their medication can change behavior. A recent study found that these patients' adherence levels increased by nearly 20 percent. What that means in practice is that most patients are uniquely motivated to improve their adherence when they see how their recent dosing histories have strayed from the prescribed dosing instructions. These results exemplify a cardinal principle of management: "what can be measured can be managed."

Capgemini Consulting: Can you describe in more detail electronic packaging?

Yes, there are different types of packages for both solid oral dose and injectables. Regardless of medication format, a smart package needs a detection mechanism for when the package is opened, a battery, and a memory of every time a patient accesses the package. Then this information is transmitted to a database, which processes patient data, then presents the information in easy-to-interpret graphs and tables.

In drug trials, we typically prefer that the data download takes place at the clinical investigator's office because of data security issues. In clinical practice, to support actual prescription of marketed products, the prescriber will need to know at the time of a patient's visit whether the patient adheres strictly to the prescribed dosing regimen.

Smart packaging acts in prevention of incorrect dosing, and also helps build habits. It is not necessary for every drug; it should be used in priority for drugs that treat serious diseases and have major potential side effects. For example, we do not really need to develop a real-time electronic monitoring system to monitor statin intake (statins are drugs used to lower cholesterol levels). But in the case of Hepatitis C, for example, if you miss one dose, there is a high risk of no response in the treatment, and also of building resistance to the drug, which then becomes a public health issue. Another example is cancer treatments, which are moving from injectables that are given in the controlled environment of the physician's office to patient-administered tablets/capsules or injections at home. In this case, patient advocacy associations are requesting smart packaging because they realize that adherence can be poor even in the case of patients with life-threatening diseases.

> *"Digital monitoring acts in prevention of incorrect dosing but also helps build habits."*

Capgemini Consulting: What would a clinical development trial look like in 3 to 5 years with a broader use of electronic packaging and monitoring?

Use of smart packaging and analysis has the potential to impact patient health by enabling optimized trial outcomes. In my view, clinical development in 3 to 5 years will rely more heavily on modeling as it approaches virtualization. I think we need to better predict through models the outcomes of clinical studies and include the effects of variable adherence as a key element of the models.

Clinical development will be done with a shorter timeline, utilizing well-constructed studies involving very select patients. The result will be faster access to treatment that will be combined with large post-market or observational studies in which adherence is closely monitored. In this approach, smart packaging with electronic monitoring will become a requirement because the broader population makes for a less-controlled research environment, for which less clinical testing has been carried out ahead of access to the treatment. I imagine regulations requiring the use of smart packaging so providers can observe patient behavior, interpret the data and use it to inform both individual treatment plans as well as broader use of the drug. Good longitudinal monitoring of both drug exposure and outcomes will allow us to derive conclusions of the drug's dose- and dosing-frequency-dependent efficacy and side effects.

Capgemini Consulting: So what does it mean for MWV?

Insights from researchers and patients allow MWV to advance packaging, data analysis and service solutions for managing non-adherence across the product lifecycle – from clinical trials to routine therapeutics in medical practice. We've seen data that show that non-adherence is largely behavioral both in trials and in clinical practice, and packaging can be a daily reminder to help patients improve their dosing behavior. Packaging, both smart and non-electronic, is an important part of an effective adherence program. We not only provide packaging but also a uniquely large database for analysis and modeling to support clinical and regulatory decision-making. We also have adherence-related science experts who have been successful in supporting our customers' clinical projects.

In some clinical studies we already provide data mining and intelligence. For example, we compute risks of patients' likelihood of early discontinuation of treatment, and we provide the healthcare practitioner with the information on non-adherence-based risks the patients can incur. MWV's Aardex Solution has been used by hundreds of thousands of patients, resulting in more than 600 peer-reviewed, published research papers. We have moved beyond selling a package to 'providing value' based on adherence: it is a huge value proposition.

> *"Clinical development in 3 to 5 years will rely more heavily on modeling as it approaches virtualization."*

Bernard Vrijens, PhD is the Chief Science Officer at MWV Healthcare and was General Manager of the AARDEX Group, prior to AARDEX becoming part of MWV Healthcare in 2012. He is also Associate Professor of Biostatistics at the University of Liège, Belgium. Bernard has co-authored two book chapters and over 30 peer-reviewed scientific papers, and was named as inventor on two patents. He is also a founding member and managing director of the European Society for Patient Adherence, Compliance, and Persistence, and is an active member of several EU- and US-funded collaborative projects around the theme of adherence to medications.

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