How Can Intelligent Packaging Best Aid Patient Compliance?

Article Written By
Chris Penfold

Published in
Pharma Sept/Oct 2010

design cognition

HOW CAN INTELLIGENT PACKAGING BEST AID PATIENT COMPLIANCE?

Patient non-compliance causes thousands of deaths and costs the healthcare industry billions of pounds each year. Innovative medical packaging can combat non-compliance and is, therefore, an area that is likely to see considerable emphasis during the next few years.

Already, advanced technology is being incorporated into packaging that allows links between the removal of medicine from packaging and the client's overall treatment plan to help improve this situation. New areas of development, such as smart materials and nanotechnology, will add to the possibilities of smart packaging, but it has to be recognized that in many areas of the world, the absence of the otherwise ubiquitous Internet and mobile phone technologies, will mean that the most sophisticated packaging advances will not be applicable. There will, however, still be a need for some levels of sophistication to combat the increasing problems with counterfeiting and to implement other aspects of brand protection. Those involved in the pharma industry will need to be up to date on the latest developments both in drugs and drug packaging.

- $77 billion for health insurers per annum USA*
- $47 billion Life Sciences Industry per annum USA*
- €13 billion in Germany** per annum
- €9.7 billion in France per annum
- €6.5 billion in Italy per annum
- €10 billion in UK per annum
- €4.3 billion in NL per annum

125,000 Deaths Annually: D. Smith, Compliance Packaging, A Patient Education Tool, American Pharmacy volume NS29, nr.2. (Feb 1998)

* Non-compliance leads to 10% of hospital admissions, Schering Report IX: The Forgetful Patient, the high cost of improper patient compliance

* L.R. Stanberg, "Drugs as a reason for Nursing Home admissions," *American Healthcare Association Journal* **10**, 20 (1984)

** 13% of all healthcare expenditure is related to non-compliance: M. Sonnenmoser, Compliance in der Arzneimitteltherapie, ABDA, (December 2002)

Figure 1: Cost of non-compliance (*Source: Rosa 2009*).

Patient Non-Compliance, Risks, Causes and Costs

Every day, millions of patients fail to take their medications as prescribed by their doctor. Medication non-adherence disrupts the healthcare system in many ways, leading to patients failing to receive full treatment benefit. Non-adherence can lead to hospitalization and even death.

The root of this problem is human behaviour. Even though we are 'creatures of habit,' we often lose momentum when taking medications or occasionally fail to understand or appreciate the benefits. Subsequently, patients often tell an 'lie' to mask the fact and avoid embarrassment, whether non-compliance was accidental or planned.

Causes of Non-Compliance

Potential causes of non-compliance are numerous, some accidental and others premeditated; the latter being attributable to a number of psychological issues. In his article, Korab, postulated that there were four causal factors:[1]

- ***Type, Seriousness and Duration of Illness:*** Spilker demonstrated that compliance is low in less serious illness cases, increases with medium level cases and drops-off again for serious cases.[1a] Also, [Heuer] that compliance reduces substantially the longer an illness persists.[1b]
- ***The Complexity of Therapeutic Regimen:*** Murray noted that: "Compliance is inversely related to the number of prescribed medications," but the frequency of the daily intake of medication also reduces the rate of compliance.[1c] Ideally, medication should be taken once daily (morning). More daily intakes cause deterioration and provoke sharp decline in compliance rates.[1d]
- ***Information about Health Condition and Trust Between Patient and Healthcare Provider:*** Compliance depends largely on health condition information and patient/Health Care Provider (HCP) trust. Generally, practitioners spend less than 60 s per prescription conveying compliance-related information to patients. Consultations usually result in a prescription, but most patients are left alone with therapy questions/concerns regarding medication benefits/risks, other drug interaction and side-effects (Heuer 1999).[1b]
- ***Health Belief Model:*** The lay patient's perception of treatment's necessity can differ completely from diagnosis and recommendations by HCP. Sometimes patients see their condition as a threat; others deny the existence of illness. Fears regarding treatment and possible side-effects will influence patient behaviour.

Risks and Costs

The risks of non-compliance can be listed on a scale of increasing negative consequence:

- ailment prolonging because ineffective efficacy levels reached
- building resistance through prolonged drug exposure leading to complete medication failure
- ailment worsening
- hospitalization
- death.

The cost, both in human lives and monetary terms, is considerable. Evidence collated by Rosa (Figure 1) estimate US and EU costs amounting to billions.[2]

Current Packaging Approaches to Limit Non-Compliance

It is widely recognized that packaging has the capability to improve non-compliance and advancing technology allows increasingly sophisticated efforts to achieve this. Many approaches have been taken, including

- Medication reminders that beep at medication time.
- Devices that track the number of dosages removed from an opened medication pack/container, collect statistics, download and check at the doctor's office or pharmacy.

- Devices reminding patients to take medications and confirmation by button pressing to send data.
- Miscellaneous alarmed reminder devices, such as automated pill boxes or wrist watches.

Although these devices can never guarantee that patients have taken their correct medicine or taken it at the right time, good packaging has a number of common attributes, including effective colour use, icons and reminder aids, accessibility, portability and robustness, plus more objective features such as 'intuitiveness.' Effective presentation of pack information can greatly ease patient use and hence encourage compliance.[3]

Examples of excellent packaging developed during recent years include

- The Zacpac (Figure 2), launched 2001 for H-Pylori patients taking three different tablets/doses per day. The solution was a single blister containing five tablets (of three different varieties) held in a 'calendared' dispensing pack. The combination of detailed instructions, therapy visualization, plus one mixed blister per day, was a real 'step forward'. It was also easier for pharmacists because it involved only one prescription, one dispensing and one explanation.
- In 2008 Stora Enso launched its DDSi (Discrete Dose Slider), a solution based on a carton with embedded Cypak Radio Frequency Identification (RFID) microchip. Supported by software enabling compliance monitoring, authentication, tracking and tracing of products, it records precise date, time and specific pill removal information. The Near Field Communication (NFC) technology is the same as that used in mobile phones and allows wireless communication between devices over a short distance, which enables functions such as electronic medication diary or SMS reminder.
- Cypak, which provides the afore-mentioned chips, has been instrumental in developing and setting global IEEE standards for wireless technology in healthcare. They have also created secure contactless technology to compete with traditional RFID systems, using conductive ink and adhesives to print electronic circuits and antennas on paper and plastic.
- Stora has recently developed a pack called 'Memori,' which also uses a microchip embedded into the paperboard, but uses conductive print.
- Protomed has developed Biodose Total Medication Management System (ToMM), which consists of patented pod and tray dispensers, sealers, alarmed cabinets, trolleys, mini-packs for community use and bespoke software (Figure3). Prepared in the pharmacy, Biodose provides the ability to dispense and monitor liquid and solid medications together, aimed primarily at compliance in the community and institutions such as care-homes, hospitals and even prisons.
- Dutch DSM TCG has developed the OtCM (Objective therapy Compliance Measurement) system, which measures and monitors patient medication compliance whilst interacting wirelessly with home diagnostic devices, correlating compliance with drug therapy (Figure 4). It monitors each individual dose taken, providing real-time data, graphs and combines medication intake and diagnostic outcomes. The technology

Figure 2

Figure 2: Zacpac (*Source: Design Connection*).

1. includes RFID labels — applied to existing standard medication blisters — which records pill removal
2. compliance information read via mobile phone, transferred to central database, then sent wirelessly to caregivers, who analyse, offering patient feedback.

These examples show the huge innovative development that has been taking place during recent years, all relying heavily on technology. So, where is all of this going?

Opportunities for Further Developments — Technology Convergence

The packaging developments above are leading edge and demonstrate the growing convergence between technology and the Internet. Fiction often prefigures reality and in the movie, *Minority Report*, a future was depicted, where visual objects are manipulated by hand, newspapers have sound and moving pictures, billboards change and interact (depending on who is viewing them) and cereal packs 'talk.' Remarkably, much of this technology already exists. Touch-screen technology is rapidly developing and 'talking' newspapers with moving pictures are close, as printing and polymer science catches up in devices such as flat-screen televisions, where Sony launched 'the world's first OLED TV' in Japan 2007.[4]

In 'Web squared,' the author refers to exponential Internet growth, as objects/devices increasingly go online, applications reside on the 'net' remotely in a 'cloud computing' environment, and the Web 'learns' by itself.[5] Objects, devices, people/things will get online directly and indirectly via vision recognition and tagging. New 'crowd-sourcing' opportunities will emerge as Smart packaging, devices and the Internet further interact to provide a more holistic approach to healthcare and wellbeing. A further result will be increasing usage of 'augmented reality' (AR), a physical real-world environment whose elements merge with (are augmented by) virtual computer-generated imagery, creating a mixed reality.

Elon University (NC, USA) made broad predictions for the future:[6]

- 2010–2014: RFID tied to GPS — everywhere. Super supercomputers. Intelligent materials.
- 2015: Adaptable materials. Genetic profiling. Human cloning.
- 2016–2025: Virtual reality (VR) immersion. Ubiquitous robots. Emotion-control devices. Paint-on power.
- 2026–2045: Space elevator. Moon base. A 'singularity' as a result of accelerating change.
- 2046–2150: Mars colony. Time travel. Brain downloading. Humans assimilated into the Internet.

So what opportunities will emerge for healthcare packaging? Certainly, it will need to be 'smarter,' not only in terms of technologies and materials, but also

- supporting changing lifestyles
- providing greater consumer and patient convenience
- lower environmental impact.

Packaging will also need to communicate better (on-shelf and at home):

- ever-more information required on ever-smaller packs
- traditional printed packaging will not cope
- use of low-cost printed displays and electronics.

Some AR technology is already used in consumer packaging, such as Lego Point-of-Sale packaging that gives a 3D visual rendition of the assembled contents within. AR needs to help solve problems for the end-user and medical packaging (patient compliance) is an avenue through which to exploit the technology benefits, help save lives and ultimately save billions of pounds per year.

Dries, however, recognized that there is 'no one-fits-all' effective compliance solution.[3] He emphasises that patients have many concerns regarding packaging used in this field; they described it as: "over-engineered," "too expensive," "not very environmentally friendly" and "very hard to recycle." There are also concerns about the 'Big Brother' nature of this intrusion, personal data-capture and information sharing, no doubt highlighted in healthcare as a result of patient information sensitivities.

Developing World Issues

The preceding devices and technologies, by their very nature, are comparatively expensive. So how could they be used in 'developing world' countries, where mobile phone and Internet access are limited and cost is a major factor in medicine use? The answer is that the very sophisticated solutions are probably inappropriate for these environments, but this is not to say that there is no role for packaging development in the distribution of medicines in less developed nations.

Non-compliance in developing nation environments has its own peculiarities/issues, often resulting in greater fatalities than the 'West.' Correct medication/dosage is one issue, but there are others, such as counterfeiting, corruption and expired products that also affect a patient's compliance and recovery.

In a report published by the World Health Organisation (WHO) in 2003, following a study on patient knowledge and compliance in Ethiopia, it was found that

- The percentage of patients demonstrating adequate knowledge (ability to tell dose, frequency of administration and length of therapy) about drugs dispensed was only 67.4%.[7]
- Adequate availability of Essential Drugs Lists (EDLs) in health facilities for six disease conditions, namely, tuberculosis/leprosy, sexually transmitted diseases, malaria, acute respiratory tract infection, diarrhoeal diseases and opportunistic infections related to HIV/AIDS was present in only 39% of 108 health facilities surveyed. So the majority of health personnel are working without standard guidelines, providing huge opportunity for incorrect drug use. Furthermore, in one region almost 50% of the medications in hospitals were found to be 'out of date!'[7]

The findings, albeit from only one African country, demonstrate a clear need for enablers, such as better packaging, to impart knowledge, promote understanding and lead ultimately to greater compliance.

It is interesting to see that the winner of the recent HCPC Compliance Packaging Awards was the Novartis Coartem malaria treatment, for a disease that kills more than 863,000 Africans annually, many children, costing $12 billion in lost African GDP.[8] It demonstrates that this area of concern is being addressed, but I'm sure that there is room for improvement. Key to Coartem's efficacy is specially designed packaging to maintain compliance via pictograms and colour coding.

This is a great initiative, but if you take into account that apparently more than 10% of drugs worldwide are counterfeit, and in some countries in excess of 50% of the drug supply is counterfeit, it opens up a number of questions. In 2003, WHO cited estimates that annual earnings of counterfeit drugs were more than $32 billion. As well as copies of real drugs, counterfeit legal drugs can include falsely labelled drugs that were previously expired, drugs where the active ingredient is fraudulently diluted, adulterated, substituted, completely misrepresented or sold with false brand name.

As things stand, there is a chance in developing nations that upto 50% of the products reaching patients aren't what 'it says on the box' — a horrifying thought. It is quite possible, therefore, that the challenge in the developing world will not be sophisticated packaging to improve patience compliance, but more likely packaging designed to combat counterfeiting and brand fraud. According to Pira International, the global brand-protection market will exceed $11.4 billion by 2014, up from $6.7 billion in 2009.[9] Pira defines brand protection as the use of tamper-evident, anticounterfeiting, antitheft, or track-and-trace technology to prevent or limit damage from brand attacks occurring through product counterfeiting, parallel trading, product tampering and theft. Smart packaging solutions will be the main vehicle for this.

Leveraging Smart Materials for Smart Packaging

'Smart' materials are those that display 'Smart behaviour,' sensing stimuli from their environment and reacting in useful,

Figure 3: Biodose packaging (*Source: Protomed*).

Figure 4: OtCM pack components (*Source: DSM TCG*).

Figure 3

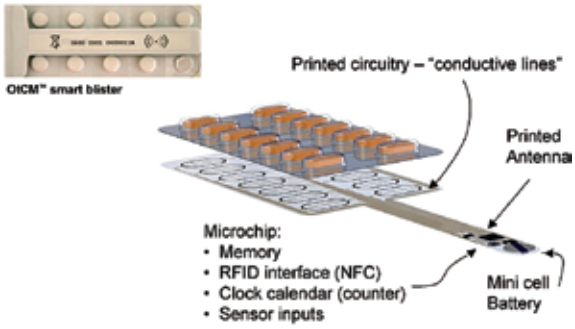

Figure 4

reliable, reproducible and usually reversible ways. Their development means continually evolving and improving capabilities. Examples are 'thermochromic' materials that change colour at a particular temperature.[10]

Affiliated is 'nanotechnology' and 'nanomaterials', involving materials at the atomic/molecular level, that can be engineered, 'designing-in' required properties — 'smart chemistry.' This includes thin-film structures resulting from deposition of multiple material layers onto surfaces to create transparent, self-assembling coatings — giving multifunctional benefits by exploiting optical, magnetic, electronic and catalytic effects.

Imagine a scenario where a pack could recognize its position (Internet connection through the packaging itself), talk to patient in their own language and explain, using sound and moving pictures, how to self-medicate. In addition, alerting pharmacists and nurses when nearing shelf-life end, to improve management of stock rotation and replenishment. It may sound similar to 'science fiction,' but much is probably already possible, although possibly not on a commercial basis.

Organic, plastic or polymer electronics, is a branch of electronics that deals with conductive polymers, plastics or small molecules, which are carbon-based, such as molecules of living things, as opposed to traditional electronics (or metal electronics), which rely on inorganic conductors such as copper or silicon.

All-organic electronic devices could be very versatile (flexible and stretchable) and because they can be deposited/printed using ink-jet or other printing technologies, could be extremely robust and low cost, providing potential to be integrated into everyday packaging. Whereas silicon chips are cost-effective only when small and produced in vast numbers, plastic electronics should be cost-effective to produce in small numbers. It should also be possible to print organic circuits on top of each other and produce large area devices similar to flexible electronic sheets made with roll-to-roll processes.[11]

Areas of particular interest necessary to provide organic electronic functionality into medical packaging include

- moving (plastic electronic) displays
- power (organic printed batteries or photovoltaic devices)
- printed sensors
- memory (organic flash memory similar to that used in a USB pen drive)
- transponders or tags such as RFID tags
- logic processors.

Things are moving forwards in all areas, but some are experiencing more R&D effort than others. Sony's New OLED screen is ultrathin (thinner than a strand of hair at 80 – µm thick) and a great example of leading-edge developments in moving displays.[12]

Conclusions

Medical packaging is an area that is likely to see considerable emphasis in the next few years. Already, advanced technology is being incorporated into packaging that allows links between medicine removal from packaging and the client's overall treatment plan, allowing patients, carers and practitioners to confirm that the right medication is being taken at the correct time. The enormous costs of non-compliance both in terms of health and health service costs will mean that considerable investment in these areas can be justified and we can expect to see continuing developments into areas such as AR, which at present seem to be simply the 'stuff of' science fiction.

New areas of development, such as smart materials and nanotechnology, will add to the possibilities of smart packaging, but it has to be recognized that in many areas of the world, the absence of the otherwise ubiquitous Internet and mobile phone technologies, will mean that the most sophisticated packaging advances will not be applicable. There will, however, still be a need for some levels of sophistication to combat the increasing problems with counterfeiting and to implement other aspects of brand protection.

The pharmaceutical industry is not always the most progressive in the uptake of technology, but demand from health services looking to save on non-compliance costs, marketers looking to minimize on brand fraud in the developing world and from health professionals looking to ensure good communication of necessary drug information to users, will ensure that there will be a continuing revolution in the packaging used for the full range of drugs on the market. Those involved in the pharma industry will need to be up to date, not only on the latest developments in drugs, but also in the latest development in drug packaging. **Pharma**

References

1. T. Korab, "Confidence in Compliance", HCPC–Europe, Packing, Packaging & Anti-Counterfeiting, *PMPS* Spring 2009, p 90
   a. Spilker – Methods of Assessing (1991)
   b. Heuer – Compliance in der Artzneittherapie 1999
   c. Murray – The Annuals of Pharmaco Therapy – 1993
   d. Haynes – Determinants of Compliance (1979).
2. D. Rosa and W. Kort, "The Achilles Heel of Healthcare: Technology Breakthrough," *Packaging Europe* (14 December 2009.)
3. T. Dries, HCPC Europe Newsletter 17, Spring 2010.
4. www.sony.net/SonyInfo/News/Press/200710/07-1001E/
5. T. O'Reilly and J. Battelle, "The Future: Web Squared (Web²)" (2009).
6. www.elon.edu/predictions/default.html
7. Assessment of Pharmaceutical Sector in Ethiopia, World Health Organisation (October 2003).
8. www.novartis.com/newsroom/news/2010-04-23_malaria.shtml
9. Pira International, *Packaging World* (May 2010.)
10. https://ktn.innovateuk.org
11. www.faradayknowledge.com
12. www.psfk.com

For more information

Chris Penfold
Chief Executive Officer
Design Cognition Ltd
Tel. +44 115 846 1914
chris@designcognition.com
www.designcognition.com