

**HCPC EUROPE
WHITE PAPER**

PATIENT FRIENDLY PHARMACEUTICAL PACK DESIGN

March 2015



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INTRODUCTION

One of the most pressing challenges facing the pharmaceutical industry today is patient compliance – how to ensure the patient takes the right medicine at the right time in the right way. Studies show that patient adherence (the extent to which a patient takes a medicine as prescribed) usually starts well but then falls away strongly over time, a worrying trend seen across almost all therapeutic areas. After 12–18 months, adherence rates may drop to around 30%, even for disease areas with very low survival rates [see Figure 1].

The impact of poor medication adherence is serious and costly to both patients and the healthcare system. Consequences include medical complications, disease progression, hospitalisations, impaired quality of life or even death. With approximately 50% of patients not taking their medications as prescribed across diseases and health conditions, moving the needle even a little toward better adherence can make a big difference.¹

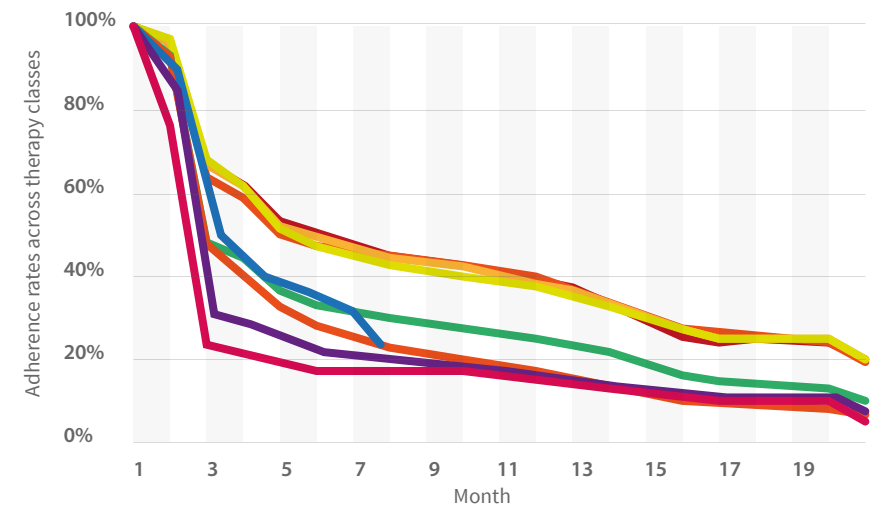
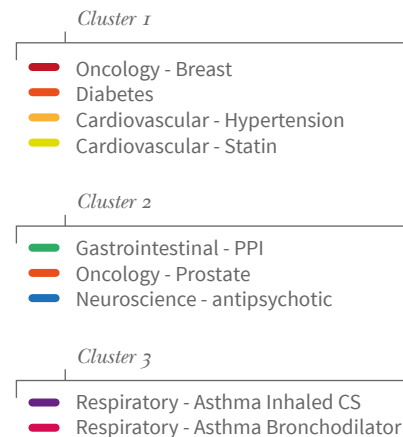
This paper aims to show how pharmaceutical packaging can have a significant impact on patient compliance and how the introduction of patient friendly packs really can lead to improved adherence rates.

Figure 1

THE SCALE OF OPPORTUNITY IS HUGE.

Cross-industry data from the US market, NDC Health.

Most dramatic drop-off between months 1-4.



ABOUT HCPC EUROPE



Healthcare Compliance Packaging Council (HCPC) Europe is a non-profit organisation established in 2004 by a group of companies involved in various aspects of the pharmaceutical supply chain, including pharma companies, packaging and machinery specialists and component suppliers. The mission of the group is to increase awareness of the need to make pharmaceutical packs patient friendly and to examine the role that good packaging can play in increased patient compliance and adherence rates. HCPC Europe occupies a position between the Marketing Authorisation Holders (pharma companies), the Regulatory Authorities (granting licences for drugs) and, most important of all, the recipients and users of the drugs, the patients themselves.

www.hcpc-europe.org



The mission of the group is to increase awareness of the need to make pharmaceutical packs patient friendly

1/

PATIENT CONCERNS

Author: *Phill Marley*



All therapeutic areas of medicine have their own individual challenges when it comes to patient compliance. Poor adherence and persistence is seen across almost all disease areas, including those for cancer and other life-threatening conditions.

Of course, every patient is an individual, with his or her own lifestyle and routines; however, studies show that most patients follow a similar emotional journey during their illness and

treatment. Unmet needs on this patient journey can cause intentional non-adherence, as illustrated in *Figure 2*.

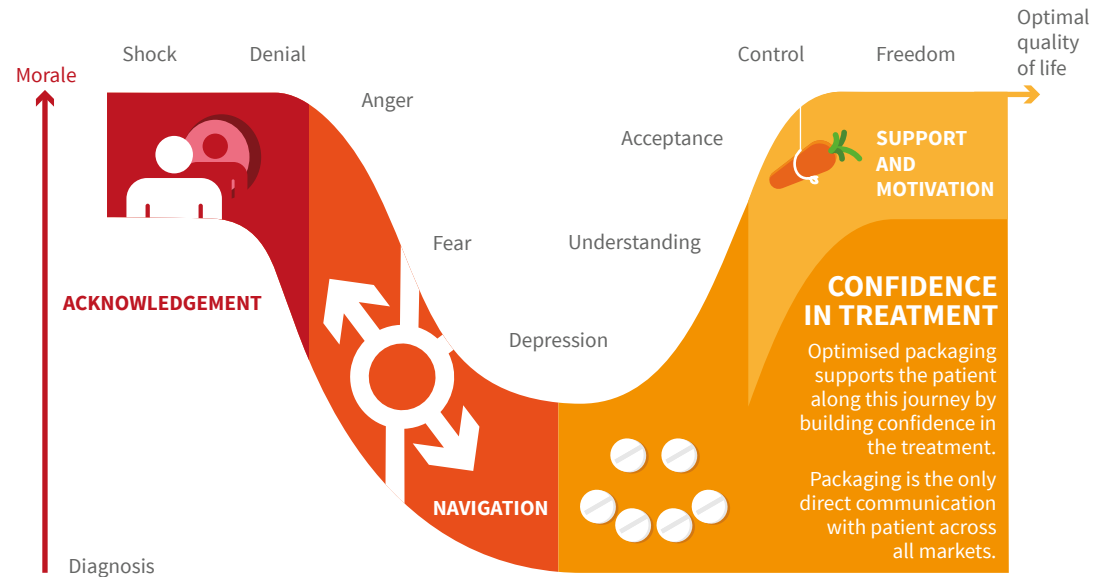
Patient friendly packaging can go a long way in assisting the patient's progress along this journey, especially in the move from depression to understanding, acceptance and ultimately control of their condition and the freedom to live a relatively normal life.

Continues.

Figure 2

THE PATIENT JOURNEY.

Evidence demonstrates that unmet needs on the patient journey cause intentional non-adherence.



1/ *Continued*

PATIENT CONCERNS



Patient insight tells us that many patients have similar concerns about pharmaceutical packaging, including the portability of the pack, the use of reminder aids and the need for clear instructions. Furthermore, many older patients find that poor packaging can be a direct barrier to compliance with medication regimens, as shown in *Figure 3*.

In reality, many of these concerns voiced by patients can be positively, and sometimes easily, addressed by the inclusion of upfront thought and sound pack design.

A PATIENT'S VIEW

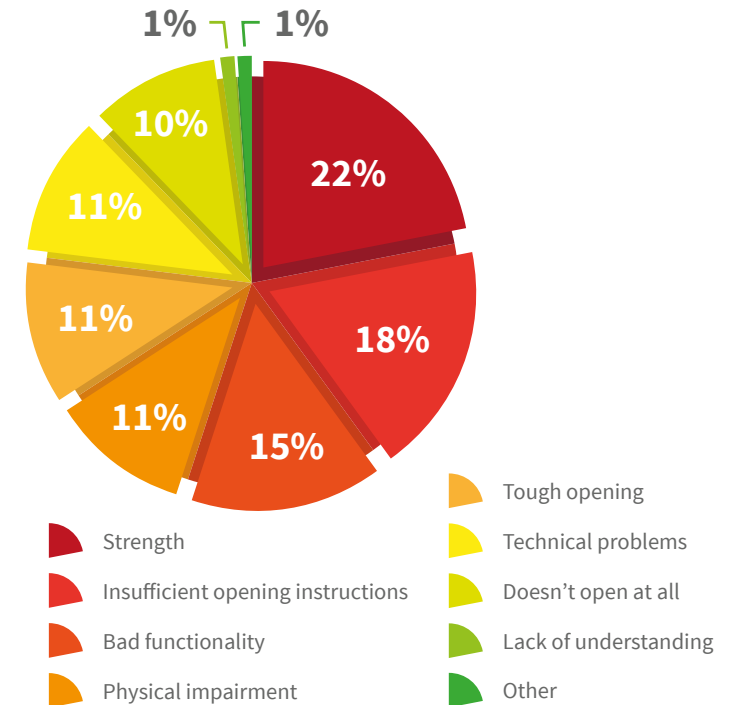
- Patients sometimes can't remember if they have taken their pill
- Poor packaging misses the job
- Blisters of ten tablets are unsuitable for a seven day/week scheme
- People do not want to disclose their disease at work with big unresectable drug packs, increasing discrimination
- Bottles are counterproductive in supporting compliance (and do not allow safe deposits of small drug supplies at work).

Excerpt from the presentation 'Patient Insights on Treatment Adherence in Oral Cancer Drugs (in CML)' by Giora Sharf and Jan Geissler, both co-founders of CML Advocates network.

Figure 3

UNDERSTANDING THE BARRIERS FOR COMPLIANCE

Problems seniors face when opening packages.



1.1/

DRUG PACKAGING AND ADHERENCE TO ORAL THERAPIES: THE PATIENT'S PERSPECTIVE

Author: Jan Geissler



Patient adherence to medication varies significantly in many diseases. Especially when treated with oral drugs in an outpatient setting, it is mostly left to the patient's own responsibility whether he or she takes the medicine as prescribed. Non-adherence - either deliberately or unintentionally - can have a significant impact on outcome, especially in life-threatening diseases like cancer.

Recent studies in a number of cancers have demonstrated a strong correlation between adherence levels, rate of relapse, rate of responses, as well as rate of hospitalisations. Furthermore, studies with electronic drug monitoring systems have also revealed that there is a significant difference between observed and self-reported adherence, suggesting that the issue cannot be adequately addressed with effective doctor-patient communication alone.

There are a number of reasons why patients fail to take their medication on the individual level, including lifestyle, psychological issues, health literacy, age and side effect issues. Beyond intentional non-adherence, for example patients taking deliberate drug holidays to reduce side effects, many patients often just forget to take their medicine or struggle to establish a routine in their

41% of patients who missed their dose accidentally did so because they forgot to take them, and 27% because their usual daily routine was interrupted

daily life. A recent study we conducted with 2,546 patients from 79 countries (<http://www.cmladvocates.net/adherence>) revealed that only one third of patients with Chronic Myeloid Leukaemia were highly adherent to their life-saving cancer drug. ^{i, ii}

To improve on adherence, compliance-aware drug packaging may play a major role. Our CML Advocates Network Study revealed that 41% of patients who missed their dose accidentally did so because they forgot to take them, and 27% because their usual daily routine was interrupted. Those with better adherence are particularly tied to their routines. *Continues.*

References:

ⁱ EHA 2013, Sharf et al., Haematol 2013; 98(s1), Abstract [1104]

ⁱⁱ ASH 2013 - Geissler et al., Blood 2013, ASH-Abstract [4023]

1.1/

DRUG PACKAGING AND ADHERENCE TO ORAL THERAPIES: THE PATIENT'S PERSPECTIVE

Patients with chronic, long-term conditions often cannot recall just minutes after administration whether they have already taken their medication. Poor packaging of drugs can increase these effects, especially in the largely geriatric population of cancer where issues like forgetfulness and co-medications are more prevalent. Daily experience with patients shows that medications provided in bottles leave minimal behavioural support to memorize the intake of medicines. Blisters of ten never match a daily schedule on seven days a week, reducing the probability to

Packaging of oral drugs can play a major role in promoting adherence. Only those drugs taken as prescribed can actually work.

develop a routine, e.g. with removing the first pill of a blister every Monday. In diseases with strong stigma, large blisters can create additional challenges for patients who do not want their condition to be known - and hence not to be seen taking their medication at their workplace. Undividable blisters do not easily allow patients to safely deposit single pills at different places, e.g. when unintentionally staying out for a night. There are many more similar effects that patient groups observe in their daily practice supporting patients to adhere to their treatment.

Packaging of oral drugs can play a major role in promoting adherence. Only those drugs taken as prescribed can actually work. Packaging may be a key cornerstone in avoiding unintentional non-adherence and driving the development of routines for regular intake. Supporting patients, and engaging with patient groups in developing targeted tools for patients to comply with their treatment, may be critical to improving health outcomes.

1.2/

THE ROLE OF MEDICATION PACKAGING IN THE IMPROVEMENT OF ADHERENCE TO PRESCRIBED MEDICINES

Author: Professor Bernard Vrijens



Poor patient adherence can manifest itself at any stage of the patient journey. For example, patients may not fill their prescription or not start taking their medication, they may not accurately follow their physician's treatment plan or they simply may stop taking their medication altogether.

There is a shared focus within the healthcare system to address the challenge of patient adherence, from government, academia, pharmaceutical companies and providers. For example, the pharmaceutical industry increased investment in adherence programmes by 281% during 2012.ⁱ However, an evaluation of 61 studies designed to improve medication adherence noted an overall increase in adherence of just 4% - 11%.ⁱⁱ Most of those programmes relied on single strategies, yet appropriate management of medication adherence requires patient-specific monitoring and support involving healthcare systems, providers, patients and their social networks.ⁱⁱⁱ

There is a shared focus within the healthcare system to address the challenge of patient adherence

A large number of existing adherence programmes are heavily weighted toward the initial prescription and refill times. These initiatives rely on physicians and pharmacists specifically addressing the issue of adherence with their patients, in addition to their other usual patient interactions. However, while provider counselling can be effective, studies show that during the medical visit, a physician will only spend, on average, eight minutes with the patient^{iv}, and 70% of pharmacists report that time is a critical barrier^v. A 2012 study showed patient adherence increased during periods of time in which patients were actively counselled, but once pharmacist-patient conversations ended, adherence quickly diminished.^{vi}

Given these time constraints and other barriers to ongoing patient-provider interaction and counselling, how can one make a positive impact on medication adherence with methods that go beyond provider interactions? Another 2012 study showed that 69% of non-adherence is behavioural, with issues such as motivation, lifestyle and forgetfulness^{vii} having more of an impact than cost and side effects. If the vast majority of programmes are focused on initiation and refill, we may be missing the opportunity to impact daily behaviour – that is, to create an appropriate habit or routine for medicine taking. *Continues.*

THE ROLE OF MEDICATION PACKAGING IN THE IMPROVEMENT OF ADHERENCE TO PRESCRIBED MEDICINES

1.2/ *Continued*



Packaging can play an important role in achieving and maintaining a medicine-taking habit. Because patients must interact with the package to gain access to the medication, the pack itself offers a daily opportunity to educate them about how to take their medication as prescribed. When medication packaging includes a well-designed calendar-style blister, it puts the patient on notice that he/she has (or not) missed some doses. This information can drive the patient's awareness and motivate the habit-building strategy. In fact, well-designed calendared blister packs have been shown to improve adherence.^{viii} Calendared packs can also help to prevent over-dosing caused by accidentally repeating the habit at inappropriate times.

In today's Internet age, patients have access to vast amounts of information and data, sometimes of questionable quality and validity. Amid this 'fog' of information, the actual medication package becomes a unique and valuable communication tool to filter and provide validated information to guide patients. Additionally, patient engagement can be enhanced by support programmes or information activated through the package. For example, a QR code or website link can connect a patient to their pharmacy or provide access to a disease management website, auto-refill programme, mobile app or loyalty programme. Packaging is effective in improving adherence when used alone, but when combined with other tactics like these, it has the potential to become even more powerful.^{ix}

References:

ⁱ *Cutting Edge Information, Patient Adherence and Compliance: Improving Outcomes Through Patient Engagement Programs.* 2012.

ⁱⁱ *Eularis Report, Ensuring Profitable Patient Adherence Programs,* 2011.

ⁱⁱⁱ *A New Taxonomy for Describing and Defining Adherence to Medications.* Vrijens et al, *Br J Clin Pharmacol*, 2012, 73(5): 691-705.

^{iv} *Block, L et al. In the Wake of the 2003 and 2011 Duty Hours Regulations, How Do Internal Medicine Interns Spend Their Time?* *Journal of General Internal Medicine.* 28(8); 1042-1047. 2013.

^v *BI Pharmacy Satisfaction Medication Adherence Pilot Final Report.* 2012.

^{vi} *Brennan, TA et al. An integrated pharmacy-based program improved medication prescription and adherence rates in diabetes patients.* *Health Aff.* 31(1): 120-9. 2012.

^{vii} *America's \$317B Condition.* *Express Scripts Infographic.* 2012.

^{viii} *A pharmacoepidemiologic analysis of the impact of calendar packaging on adherence to self-administered medications for long-term use.* *Clinical Therapeutics.* May 2011; 33(5).

^{ix} *Real-world impact of reminder packaging on antihypertensive treatment adherence and persistence.* *Patient Preference and Adherence.* 6: 499-507. 2012.

1.3/

DRUG DELIVERY AND CONVENIENCE

Author: Tassilo Korab
Professor Przemyslaw Kardas



For many patients, effective treatment adherence depends to a large degree on convenience. When initially diagnosed with a disease, patients can sometimes struggle to understand the implications of their condition and the relative treatment. Older patients often have to treat several conditions at the same time, which makes the task even more difficult.

Most diseases will have several formulation options available and the drug producer's objective will be to choose the most convenient dosage form and the easiest way of administration in order to achieve the optimal therapeutic result. Every form of administration has advantages and disadvantages, but in general oral administration ranks top on the list and is viewed as the safest, most common, convenient and economical. ⁱ Furthermore, a 1997 study with children suffering from hypercholesterolemia ⁱⁱ suggests that, amongst the oral administrable forms of medicines, pills and capsules lead to better compliance than other forms, such as powder. These forms of administration however, do require patient

compliance. An investigation based on so called discrete choice experiment (DCE) methodology, carried out recently by Prof. Kardas et al. from the University of Lodz, Poland shows that patients have clear preferences regarding shapes, sizes and colours of their solid medication. Surprisingly, their preferences for short-term and chronic treatment are not equal. *Continues.*

PATIENTS' PREFERENCES STUDY RESULTS - FORM

		THERAPY			
		CHRONIC		SHORT-TERM	
CHOICE	1 st	Capsule		Capsule	
	2 nd	Long		Round	
	3 rd	Round		Long	

References:

ⁱ Lippincotts-pharmacology-harvey-champe-5th/chapter-1/figure-1-5

ⁱⁱ Acceptability and compliance with two forms of cholestyramine in the treatment of hypercholesterolemia in children: A randomized, crossover trial, Brian W. McCrindle MD MPH FRCP(C),

Michael B. O'Neill, Geraldine Cullen-Dean, Elizabeth Helden, BSN MEd BScN MD FRCP(C), The Journal of Pediatrics, Volume 130, Issue 2, Pages 266-273, February 1997



1.3/ *Continued*

DRUG DELIVERY AND CONVENIENCE

PATIENTS' PREFERENCES STUDY RESULTS - SIZE

		THERAPY			
		CHRONIC		SHORT-TERM	
CHOICE	1 st	Small	0,00	Small	0,00
	2 nd	Medium	+12,00	Medium	+15,88
	3 rd	Large	+24,34	Large	+16,89

Kurczewska M, Kardas P, Czajkowski M, presentation at WONCA 2014

PATIENTS' PREFERENCES STUDY RESULTS - COLOUR

		THERAPY			
		CHRONIC		SHORT-TERM	
CHOICE	1 st	● Yellow		● Red	
	2 nd	● White		● Yellow	
	3 rd	● Blue		● Blue	
	4 th	● Red		● White	

Kurczewska M, Kardas P, Czajkowski M, presentation at WONCA 2014

Although there is no study that provides evidence one can assume that medicines which correspond with patients' preferences would lead to better compliance.

There are many other factors that influence patients' compliance rates, such as the number of medication intakes per day ⁱⁱⁱ. It

is known that compliance is inversely related to the number of prescribed medications ^{iv} - the more medicines a patient has to take the less likely they are to adhere to their prescriptions. But it's not just the number of medicines that makes a difference. The frequency of the daily intake of medication can also *Continues*.

References:

ⁱⁱⁱ Kardas P, Lewek P, Matyjaszczyk M. Determinants of patient adherence: a review of systematic reviews. *Front Pharmacol.* 2013 Jul 25;4:91

^{iv} Murray MD, Birt JA, Manatunga AK, Darnell JC. *Ann Pharmacother.* 1993; 27(5): 616-21

1.3/ *Continued*

DRUG DELIVERY AND CONVENIENCE

reduce the rate of compliance. Ideally the medication is taken once a day, in the morning. A twice-daily intake causes deterioration and an intake of four times or more a day provokes a sharp decline in the compliance rate.^v A meta-analysis carried out by Claxton et al concludes “*The fact that compliance with once-daily regimens was significantly higher than with 3-times-daily and 4-times-daily regimens reinforces the principle of simplicity.*”^{vi}

In order to achieve better outcomes, one of the challenges for drug makers is therefore to provide medication schemes that are simple to observe and involve as few drug intakes and as few different forms of drugs as possible. One possible improvement could be the polypill that combines several active substances (for example aspirin, statin and two blood pressure lowering medicines for patients suffering from cardiovascular problems)

and therefore reduce the number of tablets and medication intakes. An investigation carried out by Linda Bryant et al. revealed that “the participants considered that the polypill would be very convenient, especially when travelling and would reduce the pill burden.” However, “*there were concerns around the inflexibility of dosing of individual components of the polypill and some concerns about safety and efficacy.*”^{vii} Finally, even with the polypill, adherence, although better than with regular regimen, is far from perfect.

There is no simple solution to the question how drug delivery can help patients to adhere to their medication regimen, however most studies on the subject suggest that convenience and simplicity are key. Finally, even with the polypill, adherence, although better than with regular regimen, is far from perfect.

References:

^v Haynes R.B.: *Determinants of compliance: the disease and the mechanics of treatment.* In: Haynes R.B., Taylor D.W, Sackett D.L., eds: *Compliance in Health Care.* John Hopkins University Press 1979

^{vi} Ami J. Claxton, MS, Phi), z Joyce Cramer, BS, and Courtney Pierce, BA t: *A Systematic Review of the Associations Between Dose Regimens and Medication Compliance: CLINICAL THERAPEUTICS®/VOL. 23, NO. 8, 2001*

^{vii} Bryant, Linda; Martini, Nataly; Chan, Jacky; Chang, Lisa; Marmoush, Ahmed; Robinson, Belinda; Yu, Karen; Wong, Many: *Could the polypill improve adherence? The patient perspective: Journal of Primary Health Care; Mar2013, Vol. 5 Issue 1, p28*

1.4/

HUMAN CENTRED PACK DESIGN

Author: Dr Thomas Dries



The ideal pack presentation of a medicine is one that patients enjoy using and consequently want to keep using. In doing so, they are more likely to take the medicine as prescribed. The ergonomics of a drug pack is essential. Users want packaging to be easy, intuitive and reliable. When it comes to something as important as health, patients and professionals want to know that they can rely on the packed product to repeatedly perform without failures. From a patient safety perspective, the most important thing a pack must do is to fulfil the basic functionality in a reliable way.ⁱ As shown in *Figure 4*, a pack has to be functional, reliable and usable (in that order) before another layer of user-friendly design can be applied.ⁱ Among professionals in the field of industrial design there is a shared notion that “Attractive designs encourage positive responses from users”.ⁱ It is highly likely that this theory holds for the packaging of medicines as well. From this it may be concluded that the application of ‘Human Centered Design Thinking’ in the production of commercial packs may contribute to improving the wellbeing of patients.

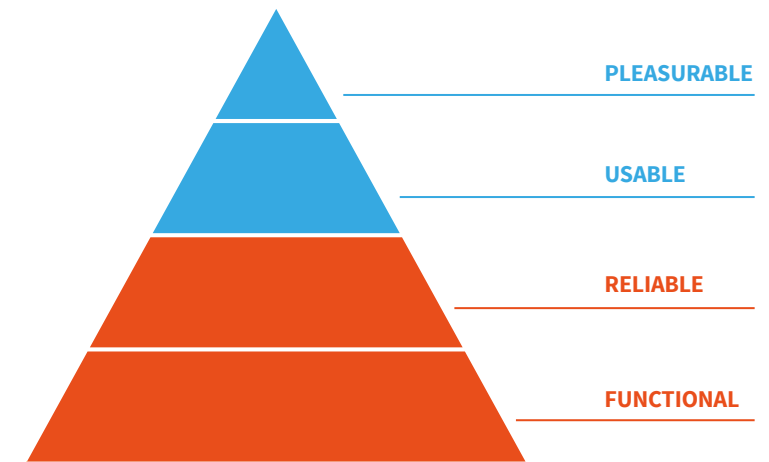
Thinking in terms of human factors is not new in the highly regulated world of healthcare. Since around 2000, the field of biologics has seen a growing focus by regulatory bodies and pharmaceutical stakeholders on the usability of combination products, medical devices and advanced drug delivery systems.ⁱⁱ The US Federal Drug Administration (FDA) expects anybody involved in launching a new medical device to consider ‘human factors’ and conduct usability validation testing to mitigate

significant use-related risks. In the terminology adopted by the FDA, considering human factors means ⁱⁱ “applying knowledge about both human capabilities (physical, sensory, emotional, and intellectual) as well as knowledge about human limitations to the design and development of tools, devices and systems etc”.

Continues.

Figure 4

AARON WALTER PYRAMID



Sources:

Aaron Walter – *Designing for Emotion*

“*Designing Human Experiences*” Whitepaper. www.havaslynx.com

1.4/ *Continued*

HUMAN CENTRED PACK DESIGN

In the meantime, human factor testing and usability measuring have become essential elements for regulatory filings of medical devices both in the EU and the US as fully supported by the European Federation of Pharmaceutical Industries and Associations (EFPIA).ⁱⁱⁱ In the field of novel drug delivery it has become common practice ⁱⁱ to apply a variety of techniques to identify use-related hazards and risks and to conduct hands-on testing to identify unanticipated hazards. The obvious drivers here are patient safety - in particular the prevention of medication errors and issues with the usability of devices. It is perhaps fair to raise the question whether there is value for adopting similar approaches in the field of packaging of oral solids such as blister packs and bottles. The outcome of a large cross-sectional study in the Netherlands ^{iv} suggests that there are still significant problems experienced by older people when opening medicine packaging. Analyzing the feedback from 317 patients to the open ended questions of pharmacy staff the Dutch research team concludes:



1. *There is a need for more patient-friendly packaging material and patient information on how to use relatively uncommon packaging systems*
2. *Furthermore, pharmacy staff should pay more attention to identifying the practical problems that people experience with the daily use of their medicines, and offer solutions to overcome these problems.*

There are similar findings in another cross-sectional study performed in Finland among healthcare workers, women with rheumatoid arthritis and elderly women. The Finnish study was geared to identify the “Critical Factors in Opening Packages” ^v and went beyond questionnaires by performing observational usability studies as well as measurements of muscular strain and ranges of motion specific to the packs analyzed. Interestingly both the Dutch and the Finnish study, despite the fact that different pack designs were analyzed and different methodologies were employed, confirmed the general findings of a much simpler study sponsored by HCPC Europe back in 2004.^{vi} *Continues.*

There are still significant problems experienced by older people when opening medicine packaging

1.4/ *Continued*

HUMAN CENTRED PACK DESIGN

From these and other studies it is probably fair to conclude that there is indeed value in taking a closer look at human factors in the context of the classical and well-established packaging of oral solids. There is much good news to share. A growing number of Pharma companies and packaging solution providers have adopted a mindset of 'Design Thinking'. This term is probably best described by IDEO founder Tim Brown in his publication Design Thinking, which lists the five personality traits^{vii} of a design thinker:

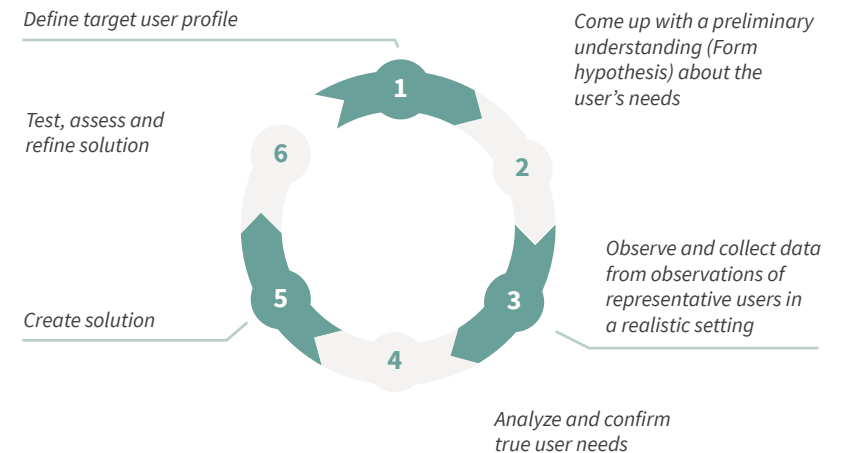
1. *Empathy*
2. *Integrative Thinking*
3. *Optimism*
4. *Experimentalism*
5. *Collaboration.*

From observations over the past decade it is clear that there is stronger collaboration and broader alignment within Pharma companies than ever before on the topic of patient centricity.^{viii} This extends to the collaboration between Pharma companies and packaging solution providers on the subject of patient-centric pack design. The focus of this collaboration is usually patient safety, in particular improvements in the reliability of packaging processes, however the foundation of this collaboration is shifting from a mainly internal focus to user needs. This goes in line with the common goal of identifying packaging processes and solutions



that provide inherently desirable features, which are capable to improving the user experience. Critical steps for arriving at pack designs which are fit for users can be summarized as follows:ⁱ

Appendix 1 Pack design flow chart



1.4/ *Continued*

HUMAN CENTRED PACK DESIGN

What looks at first glance as cumbersome, expensive and time consuming can be kept very simple. In many cases, small-scale focus group studies are sufficient to unravel criticalities in the handling of packs by patients in the context of their disease. There is no doubt; organisations that follow these processes gain critical

insights directly from the end-user, the patient. These insights enable them to produce packs that create positive user responses and in turn better outcomes of therapies, fully in line with the primary motivation for developing medicines.

Acknowledgement:

The author wishes to thank Elias Niteesh Honeywell for bringing to the attention several articles referenced here and for providing other helpful insights.

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ii *Human Factors Engineering of Combination Products and the FDA; Molly Follette Story*, PhD FDA /CDRH / ODE CaSSS CMC *Strategy Forum* - July 17, 2012; downloadable from www.fda.com

iii *Laurant Auclert EFPIA Medication Errors: Development of Prevention Strategies for Medicines and Medical Devices*, July 3, 2013

iv *Daphne Philber, Kim Notenboom, Marcel L. Bouvy and Erica C.G. van Geffen* *Int. J. Pharm. Pract.* (2014), 22, pp 200-204

v *Erja Sormunen, Nina Nevala, Sarianna Sipilä*, “Critical Factors in Opening Pharmaceutical Packages: a Usability Study among Healthcare Workers, Women with Rheumatoid Arthritis and Elderly Women; *Packaging Technology and Science*”, (2014) 27; 7 pp 559–576

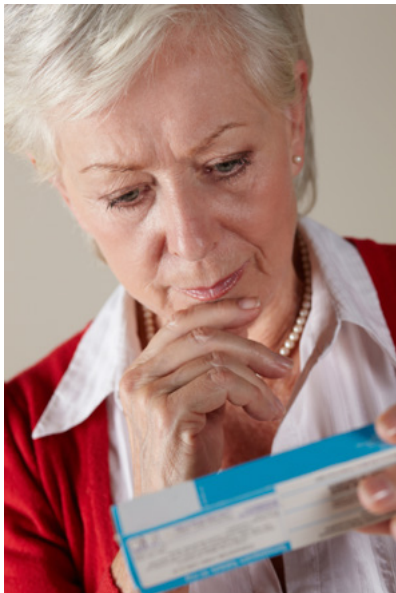
vi *Schoberberger R, Klik, K, Korab T, Kunze M*, “The influence of drug packaging on drug-taking compliance of older patients living on their own”, *Wien Med. Wochenschr.* 2007; 157 (11-12): 271-8

vii *Tim Brown IDEO Corporation*; “Design Thinking”; *Harvard Business Review* June 2008, pp 84-92

viii *eyeforpharma Healthcheck 2014* “Testing the health of the pharmaceutical industry”

2/

ADDRESSING PATIENT CONCERNS THROUGH PACKAGING



Pharmaceutical pack design has changed little over the years. Many of the medicines available in the ethical sector are still produced in the form of oral solid doses (tablets) or capsules, and these are usually packed either into bottles or in blister packs. These products are often packed in significant volumes with high-speed packing machinery that needs to be utilised over many years. As a result, most blister packs are made in a similar format, and often designs are skewed towards those that firstly provide the required product protection, and then the manufacturability aspects that the packing lines require. The balance between manufacturing demands, regulatory constraints and the needs of the patient need to be carefully considered.

Other medicine presentations such as metered dose inhalers (MDIs) or injecting devices make it inherently easier to comply with required dosing, and in some cases the dose may even be administered by physicians or carers.

As we shall now explore, there are aspects of the component parts of a self-dosing patient pack that if well designed, can assist that patient in the best compliance and adherence regimes.

The balance between manufacturing demands, regulatory constraints and the needs of the patient need to be carefully considered

2.1/

EASE OF ACCESS TO CONTENTS

Author: Prof. Dr. Felix Ecker



Packaging is the product's face. It protects the packaged goods and is an important aspect of brand identity. It presents the product and displays important information. If it's good, packaging can successfully initiate a purchase.

Unfortunately, the role of packaging is too often reduced to these points. But packaging has a second face, which is unveiled when the customer tries to retrieve (or sometimes wrestle!) the product out of the pack. This is a critical situation, not only for momentary customer satisfaction, but also for future purchase decisions. According to a 2003 study, the majority of 'Silver Agers' face challenges with the opening of consumer products. For them, this is almost a part of daily life but the experience can influence their decision making at the point of sale. Many senior customers are willing to change the product and brand if there are alternative products with easier to open packaging.

This is just as true, and equally important, for pharmaceutical packaging. If patients cannot open the packaging of their products, how can they adhere to their therapy regime? This is certainly not fostering compliance.

It is critical that the industry keeps this in mind when developing future products and packaging. To do this in an efficient way, it is vital to understand where the problems lie so that new solutions can be created. Although a panel test specification for consumer products exists (CEN/TS 15945), it is hardly used.

So does this mean we are afraid of our customers?

This panel test can inform much more than just delivering a yes/no result. With expert observers, we can unearth significant information about packaging handling, from cognitive challenges to mechanical forces and accuracy.

So far, it is hard to predict the influence of changes in packaging, even minor ones, on the ease of opening. In a project at Hochschule Fulda, University of Applied Sciences, correlations between results of panel tests and technical testing methods are being researched. It is hoped the studies will help to predict the ease of opening based on mechanical parameters. Panel tests cannot be replaced, but it will help to bring the ease of opening into early packaging development.

Researchers at Hochschule Fulda have developed in-depth expertise on how to apply CEN/TS 15945 in an optimal way and how to maximize the learning from it. The team has developed a test protocol that provides detailed information on critical aspects and potential challenges of packaging. This knowledge can directly influence the product concept and provide the expertise to develop packaging tailored specifically for 'Silver Agers'.

2.2/

ARE MEDICINE PACKS REALLY UNFRIENDLY?

Author: Professor Karel van der Waarde



Small cardboard boxes, impenetrable blister packs, child safe caps and multiple folded instruction leaflets on biblical paper with Lilliputian type do not seem to be designed with patients in mind. Medicine packaging – like some other forms of packaging – appears to prevent simple access. It is usually hard to handle and is often difficult to use. Could this just be a general but incorrect assumption, or should this be a fruitful area for improvements and innovation? How can this ‘patient friendliness’ be investigated, and if the performance is lower than our expectations, how can it be improved?

STEP 1

Unfriendly for whom? Which activities? Which medicines?

As a first step, it seems worthwhile to ask which packaging and which groups of patients need attention. It is unlikely that all medicine packaging and all patients are equally problematic, we should look at three factors: activities, patients, and medicines.

For patients, selecting the correct medicine pack in a drawer, opening and reclosing the pack, remembering to take the medicine on time, checking if the medicine has been taken, carrying the medicine and finding contact details in case of an emergency are all important activities. For each action, it is necessary to consider the additional difficulties faced by patient groups with specific characteristics, such as colour blindness, poor eyesight, lack of dexterity, reading difficulties and language barriers. Some of these characteristics can change during the use of a medicine.

There are major differences between medicines too. For example, there are differences between ‘over-the-counter’ and ‘prescription-only’ medicines; between medicines for chronic illnesses and for short term use; for use in hospitals or at home; and for use in emergencies or in tranquil environments. The combination of ‘a particular patient’ who needs ‘to do something’ with ‘a particular medicine’ is the central core of ‘patient friendliness’. If one of these factors changes, the other two will be affected. *Continues.*

It is unlikely that all medicine packaging and all patients are equally problematic; we should look at three factors: activities, patients, and medicines

2.2/ *Continued*

ARE MEDICINE PACKS REALLY UNFRIENDLY?



STEP 2

Apply a process that really enables people to act appropriately

The combination of different users, characteristics, medicines and actions seems very hard to tackle. The discussion around patient friendliness of medicine packaging can become complex but it is important to recognise that there is no standardized optimal solution for all situations. One possible approach to tackle this variation is based on ‘Design Thinking’, discussed in chapter 1.4.

This approach starts from an intention to change, based on a critical assessment of the requirements of all the different people involved. The aim is to consider all the actions and enable each user to conduct these actions as well as possible. *[Note: This is in conflict with the current EU-legislation which starts from the assumption that there is only one single user, and that standardization is beneficial for all.]*

STEP 3

***What do people need to do?
Which actions are most problematic?***

To determine whether a modified design will increase the patient friendliness of a package, each of the actions of a patient needs to be considered and benchmarked. For some medicines, it might be more important to look at regimen schedules in order to help patients to remember to take the right dose at the right time. For others, it might be the ease of opening a blister pack, or to extract the right amount of liquid from a bottle.

It is essential to look at particular medicines in particular situations and prioritize the actions that need attention first. Problematic actions can be identified and tackled by starting from a collection of available products (‘how did others approach this?’), benchmarking examples (‘which ones are really better?’) and then retesting in different circumstances (‘would this work for our product and our patients?’). *Continues.*

2.2/ *Continued*

ARE MEDICINE PACKS REALLY UNFRIENDLY?



STEP 4

Design for each action

The design task focuses initially on ‘one action for one patient in one situation’. Ideally, a combination of the following five different approaches should be considered:

1. *The system of providing a specific medicine to specific patients*
2. *The processes that are involved in this provision*
3. *The availability of training and support*
4. *The physical design of visible objects*
5. *The provision of information and instructions*

The combination of these five approaches can really modify a situation into a preferred one.

STEP 5

Test and redesign

It is unlikely that the first prototypes will immediately increase patient friendliness across several actions. Patients might misconceive good ideas and minor reactions during test-interviews might open completely new development avenues. Designing, testing and redesigning is a long-term process and step-by-step progress can lead to verifiable increased performance.

CONCLUSIONS

The main point is that best practice of patient friendliness does not focus on standardised results, but on a process of continuous critical observation and change. Each of the five steps mentioned above provides opportunities to optimally support the actions of patients in specific contexts. Each activity needs to be considered and designed to enable patients to act appropriately. If medicine packaging follows these steps, then opening a medicine package might even become a pleasant experience.

2.3/

USE OF ICONS AND COLOURS

Author: Andrew Love



THE USE OF COLOUR

Among the arsenal of techniques to improve the design of product packaging, two powerful tools are the use of colour as a differentiator and highlighter and the use of icons to clarify instruction or provide specific information. Conversely, the incorrect use of colours and icons can be a significant contributor to poor packaging design.

In this next section, we will look at how colours and icons can aid the design of packaging and the provision of information.

1 / THE USE OF COLOUR TO IDENTIFY PRODUCTS

Where a manufacturer has a number of products being offered with a similar standard company branding, colour can provide a method of differentiation between these products. This can be particularly beneficial where the brand or generic drug names are similar, as shown on the example here. However the sheer range of pharmaceutical products on the market makes associating a specific product with a specific and unique colour impractical, if not impossible. *Continues.*

Proprietary Name 1
NameOne

500mg
(as sodium salt)

Powder for solution
for injection/infusion.

Each vial contains
Name One sodium
equivalent to 500mg
of Name One.

For intramuscular
and intravenous use.

Proprietary Name 1
NameTwo

500mg
(as sodium salt)

Powder for solution
for injection/infusion.

Each vial contains
Name Two sodium
equivalent to 500mg
of Name Two.

For intramuscular
and intravenous use.

USE OF ICONS AND COLOURS

2.3/ *Continued*

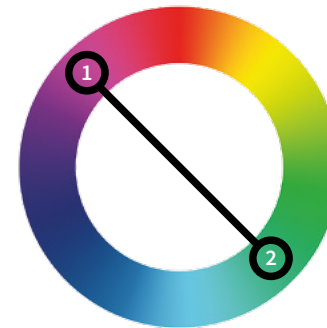
2 / THE USE OF COLOUR TO DIFFERENTIATE BETWEEN STRENGTHS

Colour can also be powerful in ensuring that the strengths of the same product are clearly different. The use of a clear and contrasting colour palette will assist in ensuring that the different product strengths are clear when stored together. To ensure a high contrast between colours, the principle of a colour wheel, and choosing opposite colours on the wheel, can be beneficial.

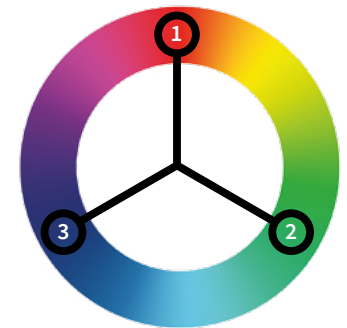
Continues.

<p>Proprietary Name Generic Name Tablets 10mg 28 Tablets</p>	<p>Proprietary Name Generic Name Tablets 20mg 28 Tablets</p>
<p>Proprietary Name Generic Name Tablets 30mg 28 Tablets</p>	<p>Proprietary Name Generic Name Tablets 40mg 28 Tablets</p>

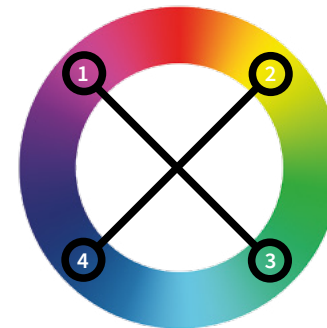
2 COLOURS REQUIRED
(example)



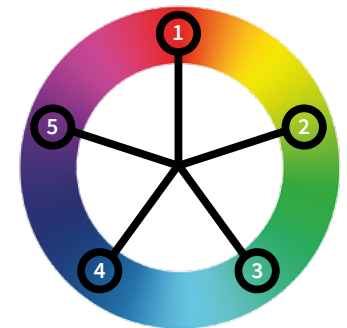
3 COLOURS REQUIRED
(example)



4 COLOURS REQUIRED
(example)



5 COLOURS REQUIRED
(example)

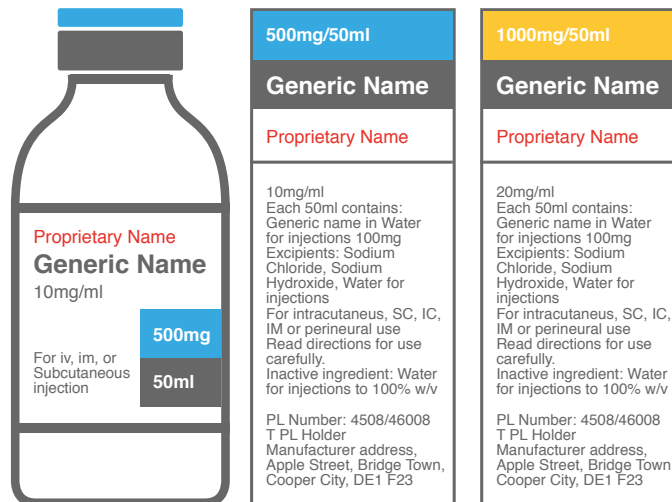


USE OF ICONS AND COLOURS

2.3/ *Continued*

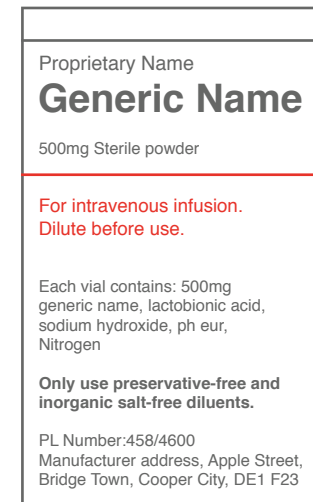
3 / THE USE OF COLOUR TO ALIGN COLOURS ACROSS COMPONENTS

Where the company has a product with a number of components and strengths, it makes sense to align the colours across the components for a particular strength. This helps to avoid confusion.



4 / THE USE OF COLOUR TO HIGHLIGHT KEY ELEMENTS OF TEXT

Highlighting text in a different colour, e.g. red, is beneficial in helping to draw attention to highly important statements that pose significant risk, for example the need to dilute or product for paediatric use. *Continues.*



2.3/ *Continued*

USE OF ICONS AND COLOURS

5 / THE USE OF COLOUR TO CONTRAST FOR READABILITY

To assist readability, it is important that there is a strong contrast between the colour of the text and the colour of the background. Grey text on a grey background is not going to be helpful to a healthcare professional in a night-time hospital ward.

SOME CAUTIONS ON THE USE OF COLOUR AS A SOLE DIFFERENTIATOR

Whilst it can be seen that colour has a significant role in assisting with the differentiation of products; there are some shortcomings that must be considered. Firstly, colours can look different in certain lighting conditions. Secondly, people have different perceptions of colour. And thirdly, colour blindness can result in some people seeing colours differently. Therefore designers should use multiple approaches to ensure differentiation rather than rely on colour alone.

THE USE OF ICONS

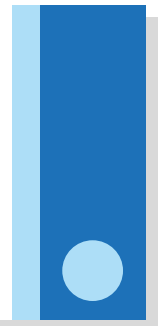
There are two main uses for icons on pharmaceutical packaging - the application of symbols required by specific legislation and the use of illustrations to aid instruction. *Continues.*

Proprietary Name

Generic Name
Capsules

10mg

28 Capsules



Proprietary Name

Generic Name
Capsules

10mg

28 Capsules



2.3/ *Continued*

USE OF ICONS AND COLOURS



LEGISLATIVE SYMBOLS

Many legislators require certain symbols to be added to pharmaceutical packaging. These include, for example, the recycling symbol (left) which must be shown on packaging in some countries. Where symbols have to be applied for legislative purposes, it is important to ensure that the correct symbol is being applied and that if the packaging component is used in other countries, there is no issue with showing the symbol if it is not required.

INSTRUCTIONAL ILLUSTRATIONS

Article 62 of European Commission Directive 2001/83/EC permits the use of images, pictograms and other graphics to aid comprehension of the information provided with pharmaceutical products. However the inclusion of any elements of a promotional nature is excluded. Illustrations can be useful in clarifying and highlighting aspects of the instruction but they should not replace actual text. Furthermore, evidence may be required to ensure

that their meaning is generally understood and not misleading or confusing. If there is any doubt about the meaning of a pictogram it will be considered inappropriate. Particular care will be needed when symbols are transferred or used in other language versions of the leaflet and further user testing of these may be necessary. In addition, companies are likely to have developed illustrations over many years for different requirements. It is therefore essential that processes are in place to ensure correct illustrations are applied, unwanted illustrations are no longer used, and the range of illustration is maintained at an effective and minimised number.

SUMMARY

As we have shown, colour and icons can provide solutions to ensure differentiation, readability and understanding of pharmaceutical products. However they cannot be considered stand-alone answers but are part of a toolkit of techniques available to the packaging designer to create effective patient safe packaging designs.

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2.4/

PORTABILITY AND DISCRETION

Author: Phill Marley

PORTABILITY

Many patients need to take their medication with them when they travel. This means packaging needs to be portable and compact. In many cases, this is a straightforward requirement, as some presentations/doses are small and easily contained in a small package, which also needs a certain level of durability.

For tablet products provided in blister packs, consideration should be given to the size of each blister strip, and whether a number of smaller strips would be more suitable with the required dosing regimen, e.g. 4 x 7 strips rather than 2 x 14 strips. Perforations in blister strips can also be useful as they allow sub-division of larger strips and therefore increased portability for a small number of doses; say over a holiday weekend.

Blister strips using formed aluminium foil or laminate for the base layer usually take up a bigger 'footprint' than those made from flexible films, because of the limitations in the depth and gradient of pocket size that can be achieved with this material. Larger packs are not favoured by patients or pharmacists, so for products requiring a high barrier to moisture, producers should consider the use of high-barrier films instead, as these materials allow the production of smaller footprint blisters whilst still providing high moisture barrier properties.

The physical design of the carton can also assist with portability requirements, with a number of novel packs allowing easy fit into a pocket for storage, and easy access to both the medication and the patient information. Bottle packs need to be small and easily stored for travel, with consideration given to the use of flat, easy to store designs as well as traditional round or square shapes. Other presentations like inhalers, injector pens and the like are complete units and usually compact in nature anyway. *Continues.*

Blister strips using formed aluminium foil or laminate for the base layer usually take up a bigger 'footprint' than those made from flexible films

2.4/ *Continued*

PORTABILITY AND DISCRETION



DISCRETION

Many patients desire a discreet pack so they can take their medication without drawing attention to themselves or their illness. Often doses need to be taken more than once a day and this can mean that medication is present in some social situations, like an evening out with friends. With this type of dosing regimen, consideration to 'lifestyle packaging' is important – for instance, packs with friendly, stylish shapes with modern non-clinical designs.

Size is definitely an issue here. Patients tend to favour small, easy to carry packs or sub-dividable packs, even if they have to split them themselves. The key message is that medicines should fit in with the patient's life, rather than the other way round. In addition, thought should be given to the design of the pack, in that some presentations which are well designed and ergonomic will draw less attention and therefore allow the user to take their dose in a more private way.

2.5/

COMPLIANCE AND REMINDER AIDS

Authors: Thomas Sefrin &
Stefanie Meier



Taking (prescription) drugs regularly can be a complex and demanding task, especially if the dose regimens affect the individual's everyday life and activities. As a result, some people (if not most) do not follow the agreed medication regimens to the extent that is required. Non-compliance could be both intentional and non-intentional.

NEED-ORIENTED FEATURES IN PACKAGING DESIGN

With little additional cost and design effort, packaging of medicine can support adherence and compliance, improve therapy outcomes and make a difference in patients' lives, therefore contributing to decreasing overall healthcare costs. By incorporating adherence features in the structural and graphic design of packaging, some individual, patient related factors of non-adherence can be addressed.

Need-oriented packaging design offers opportunities to increase the effects of the therapies. On the other hand, packaging with special features has to prove its functionality if it is to be used to support and organize the correct intake of drugs. Such packaging has to communicate in a clear and unambiguous way the information to guarantee reduction or prevention of medication errors. ⁱ

One of the unintentional reasons for non-compliance is that patients or caregivers do not understand prescribing information correctly. A goal for adherence support therefore should be to intuitively reflect the prescribing information and dose regimen in the packaging design. There are three levels in packaging design that offer this opportunity:

1. *The structural design of primary packaging (the container and closure that is in direct contact with the drug)*
2. *The structural design of secondary packaging (in most cases a folding box or bundling box made of carton board)*
3. *The graphical design which is printed or labelled on the primary and secondary packaging.*

Instructional and graphic designs are important communicators for patient safety, explanations of administration and instructions for use. Guiding the patient visually to the important information can help them to better understand the correct way of taking the drug. *Continues.*

COMPLIANCE AND REMINDER AIDS

2.5/ *Continued*



One of the most common and cheapest options to support adherence in medication packaging is to print the lid foils of blister packaging to coincide with the days of the week. This concept, known as ‘calendarisation’, has been well known since the introduction of the birth control pill.ⁱⁱ The use of illustrations or pictograms can also make a difference by bringing critical information to the fore in the artwork of secondary packaging.

Some ideas for reminder aids in the primary blister packaging include:

1. *The blister configuration itself, if a logical number of cavities per blister reflects the dose regimen (e.g. two capsules in the morning and two capsules in the evening)*
2. *Routine development, allowing patients to form routines by, for instance, taking a new blister strip every day (daily routine) or switching to a new blister every other 7th day (weekly routine)*

Examples of adherence features in structural design of secondary packaging include:

1. *Compartments in the bundling box to divide the monthly supply into logical parts, e.g. seven days per compartment*
2. *Incorporated windows to show the remaining amount of product in the pack (a reminder feature for the next prescription)*
3. *Defined spots for positioning different elements of the pack assortment to reflect the right order of starting a medication (e.g. first read the instruction leaflet, then prepare your medication e.g. dilute the tablet in water)*
4. *Additional panels added to a folding box offer the possibility to print e.g. calendars or instructions and therefore in combination with the artwork support patient’s adherence.*
5. *Wallets as customized structural packaging systems, offering opportunities to support the patient in its adherence by combining graphical design with structural design. *Continues.**

COMPLIANCE AND REMINDER AIDS

2.5/ *Continued*



REMINDER FEATURES FOR ADHERENCE SUPPORT

Scientific reports have tried to quantify the value of reminder features in packaging to support adherence in patients. Reminder features in packaging can look very different, they may appear not only on unit-dose packaging such as blisters, but also in bottles, pill organisers or wallets. Reminder features offer an integrated solution to plan and track the intake, to control if the intake took place or to show if and when the medication should be taken next.

Reminder features may require some active involvement and interaction by the patient with the product packaging by pushing through, crossing through or removing the reminding feature. The reminding features may also support documentation of the intake, which is beneficial as self-estimated adherence is often higher than it may be in reality.ⁱⁱⁱ

Despite their familiarity, bottles have been proven to have lower adherence rates compared to other types of packaging. A bottle is a well established form of packaging, common in everyday life, but the opening and reclosing of a bottle can happen so intuitively and automatically that it can be hard to remember whether the cap of the medicine bottle was already opened or not.ⁱⁱⁱ

A recent study has shown that calendar blister packaging can have a positive effect on the refill rate of prescriptions compared to the same medication in plastic bottles. Newly diagnosed patients who have not yet establish a medication management routines are particularly able to profit from calendarized packaging.^{iv} On the other hand, the study also showed that calendarized blister packaging does not generally bring positive effects, for the simple reason that “one size does not fit all”. In effect, patients with already established routines do not generally profit from calendar packaging in the same way that new patients do. What’s more, patients who take various medications simultaneously can get irritated with calendar packaging if they are used to managing their drugs otherwise. But the study did not find negative effects of the reminder features on the adherence.^{iv} It can be assumed therefore that reminder features either support patients in being adherent or, as a worst case, have neutral effects on adherence. For these reasons, it should be one of the objectives to integrate reminder features in packaging systems as part of a versatile adherence strategy. *Continues.*

COMPLIANCE AND REMINDER AIDS

2.5/ *Continued*



A relatively broad study carried out in the US^v showed that the adherence to a hypertension therapy packaged in calendar blister packaging was significantly higher compared with the product packaged in bottles without reminder features. The study results show that the medication possession ratio (MPR) in calendar blisters resulted in 80% versus 73% in standard bottles. The MPR gives the portion of the amount of days where the medication is available to the overall days (in case of the study this was 11 months). The conclusion is simple: The higher the MPR, the higher the probability that the patient takes the drug and thus is adherent to the dose regimen.

Evaluations should show the influence of investments in need-oriented packaging in the context of the added value for patients in terms of their medication management. It is important to acknowledge that need-oriented design is only feasible if the needs of patients as well as product and dosing requirements are clear. The objective we should always have in mind when designing drug products is that patients who are more compliant to their medication have a higher probability of being adherent and thus reaching therapy objectives and are less associated with additional costs for treatment of medication errors or side effects.

CONCLUSION

Sources:

ⁱ Heneghan, C.; Gasziou, P.; Perera, R.: *Reminder packaging for improving adherence to self-administered long-term medications (review)*; The Cochrane Collaboration, Wiley & Sons, Issue 3, 2008

ⁱⁱ Gossel, *Packaging the Pill*

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^v Dupclay, L.; Eaddy, M.; Jackson, J.; Raju, A.; Shim, A.: *Real-world impact of reminder packaging on antihypertensive treatment adherence and persistence*; *Patient Preference and Adherence*, number 6, pages 499-507, Dove Press, 06.2012. DOI: 10.2147/PPA.S31417

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3/

REGULATORY CONSIDERATIONS FOR PACKAGING DESIGN - CREATIVITY VERSUS SOLIDITY

Author: Nabeela Butt



The pharmaceutical industry is one of the most regulated sectors in our society. However, there is increasing concern that, apart from all the benefits of drug regulations to patient safety, the balance may have shifted towards over-regulation with apparent threats to drug innovation. The need for regulation is not in doubt. The aim is to ensure that medicines arrive safely in the hands of the patients for whom they are prescribed.

Opinion sometimes considers packaging to be superfluous. However, it must be emphasized that packaging preserves the stability and quality of medicinal products and protects them against all forms of spoilage and tampering. All medicinal products need to be protected and consequently need to be packaged in containers that conform to prescribed standards, particularly with respect to the exclusion of moisture and light and the prevention of leaching of extractable substances into the contents and of chemical interaction with the contents.

So we now have the classic comparison of apples and oranges, or in this case the comparison of packaging 'creativity' versus regulatory 'solidity'.

The focus for the packaging design engineer will be on creativity and the desire to make things easier for patients – easier to open (or sometimes, less easy to open), secure, engaging, tamper-proof, clear etc. But at some point a colleague will inevitably ask “have you considered the regulatory requirements?” and at this point

the designer's face will drop as he/she realises the impact they will have on his/her wonderful design solutions!

So who will win in this scenario – creativity or solidity? The answer is simple. Neither will win, because in the current regulatory framework, there is not much room for creativity. Novel pack designs start to fall under what is termed 'the grey area' of regulatory. Design very rarely fits within the black or white words that make up the regulations.

However all is not lost. Regulatory Affairs processes can help rather than hinder the packaging design. Labelling is an ideal example. You can work with regulatory colleagues to create a label that is relevant, clear and precise; one that will help the patient to understand the complex nature of the patient information leaflet. And then you have the more obvious external packaging (carton, blister, bottle label). Again regulatory colleagues can give guidance on the potential for layout, terminology, logos and anything else that can enhance the message being conveyed to the patient via the packaging. So engage with your internal regulatory colleagues early in the development process, not at the end when you have already defined the solution. With early engagement, you can better develop the right design with the right features and ultimately have a greater chance of gaining regulatory agency approval. *Continues.*

REGULATORY CONSIDERATIONS FOR PACKAGING DESIGN - CREATIVITY VERSUS SOLIDITY

3/ *Continued*



Each regulatory agency has its own dictate on packaging and its applicability to the overall regulatory framework, so be sure to use your internal regulatory colleagues to engage with the agency beforehand to explain your design. This may not be necessary for all situations but with complex proposals it is always advisable to engage early to set the scene and establish the scope in which you can and cannot work.

Remember that regulators like to be involved and like to help. It is a common misconception that regulators are not flexible in their approach and this is no more evident than in the Escher project.*

This project is looking at improving the EU system for marketing authorisation and learning from regulatory practice.ⁱ The Escher Project initiates research and policy debate on the development, marketing authorisation, reimbursement and use of medicines. Its goal is to facilitate patient access to medicines and innovative technologies that address public health needs. This example shows that regulatory agencies want to engage with industry to improve their processes and to become more of a partner in discussions relating to a product development.

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ⁱ <http://escher-projects.org>

** Escher is TI Pharma's multi-stakeholder platform for regulatory science and dialogue. Currently, Escher is in the final phase of a project that explores a number of perceived bottlenecks in the regulatory system. The project will result in a wealth of information for regulatory improvement to benefit the development of products addressing priority medical*

needs. On September 18th, Escher will launch the resulting project report in Brussels at a joint DIA/TOPRA event. The project was jointly funded by EFPIA and AESGP. TI Pharma's contribution ensured that all project partners could operate in an independent manner and that relevant stakeholders were consulted.

4/

SEMIOTICS

Author: Phill Marley

Semiotics, or the study of signs and signalling techniques, both conscious and unconscious, is too big a topic to be discussed in any detail in this paper. Nevertheless, when designing pharmaceutical packaging, the visual appearance of a pack can make a considerable difference to how a patient views their medicine, their condition and even the company that makes the product. The feelings created by the pack, the colours, the typography, the pictures and the words all have an effect on the user.

The use of colour has already been discussed in this document, but in a differentiating context. Colours also play an important role in our emotions. Typically, creative use of colour is underutilised within the pharmaceutical industry, which predominates with dark blues in the belief that the colour implies distance and authority. Purples say depth, moodiness and death, whilst black also stands for death. White can be neutral or clinical, with red signifying blood and emergency, but also speed, verve, and in some cultures, celebration. Green is calming, yellow creative and optimistic, while lighter blues convey knowledge and communication. Careful consideration of the use of colour can pay dividends, and in particular, brighter colours, as these can lift the spirits, give the patient hope and make them feel better.

Much of the pack imagery found in the current pharmaceutical marketplace conveys pessimism, intimidation and hard, clinical appearance, when the patient would be much better served with authoritative, approachable images that reinforce positive

feelings. Often, heavy black sans serif fonts are used, and these present a cold, characterless, domineering or aggressive image. Use of a lighter touch can prompt gentle confidence and authority; a sense of individuality, reassurance and balance.

Emotional engagement with the patient can be achieved by the use of visual metaphors, and there are many examples of these to be found. A new plant shoot signifies hope and a new beginning, a splash and a ripple implies endless possibilities and water droplets on a leaf point to freshness, cleanliness and renewal. Use of this type of graphic can be a powerful way to communicate emotions and instil upbeat feelings like resurgence, expectation and optimism.

A high level consideration of semiotics and the benefits it can bring to a pharmaceutical pack is thoroughly recommended.



5/

THE FUTURE OF ELECTRONICS IN DISEASE MANAGEMENT

Author: Professor Bernard Vrijens



SMART PACKAGING

Medication adherence feedback that changes behaviour and enhances adherence

As previously outlined, the reasons for patient non-adherence are primarily behavioural. One way to create real, lasting change in patient behaviour is to build a habit, i.e. a choice that we deliberately make at some point and then stop thinking about, but continue doing at appropriate intervals, often every day. Habits are an important aspect of human behaviour, writes Charles Duhigg in his recent bestselling book called the “The Power of Habit.”ⁱ Duhigg states that habits makes up 40% of our daily routine.

Behavioural change and habit formation are extremely important in the first 90 to 180 days of starting a medication, which includes the filling and dispensing of the first prescription, and often two subsequent refills. Forming and supporting positive medication-taking habits from the onset of therapy will result in enhanced patient adherence. One way to influence behavioural change and potentially help create a habit is to show patients how well or poorly they’re taking their medication over a period of time. A recent systematic review of the literature by the EU-sponsored “Ascertaining Barriers for Compliance (ABC) project” (www.ABCproject.eu) found that providing patients with feedback about their own adherence patterns made more of a difference in adherence than any other adherence-oriented intervention.ⁱⁱ

To provide real-time feedback to patients, providers can utilize electronic ‘smart’ medication packaging. This type of packaging provides a reliable and detailed measurement of patient adherence to prescribed medications. Smart packaging can be customized for various medication regimens and is available in different formats for inhalers, injectables and solid oral dosage forms. Regardless of the medication format, a smart package includes a detection mechanism for when the package is opened or activated and a memory record for every time a patient accesses the package. For example, Medication Event Monitoring Systems (MEMS) have been used with more than 500,000 patients and their use has been reported in over 600 peer-reviewed publications. Studies have shown that when a patient accesses his or her MEMS package, there is an extremely high likelihood that the drug will be taken. In fact, research has shown less than 3% discrepancy between opening the package and swallowing the pill in the case of orally administered drugs.ⁱⁱⁱ *Continues.*

Studies have shown that when a patient accesses his or her MEMS package, there is an extremely high likelihood that the drug will be taken

5/ *Continued*

THE FUTURE OF ELECTRONICS IN DISEASE MANAGEMENT



The detailed data provided by smart packaging allows for a focused discussion between patient and provider that can help to identify specific adherence barriers and develop an action plan for overcoming challenges. An adherence assessment can be especially important when a patient's treatment fails to act as expected. Adherence patterns can help providers better understand both the underlying and fundamental reasons for treatment failure, including inappropriate dosage taken, the medication itself, or non-adherence to the medication's dosing regimen. This understanding at the point of care may lead to more successful patient treatment, better patient health outcomes and reduction in healthcare costs.

Smart packaging is most commonly used now during drug development,^{iv} but in looking to the future, we foresee broadening use in both clinical trials and medical practice. In 2012, the US FDA provided guidance about smart packaging in drug development, which stated: "Practices such as... using 'smart bottles' to monitor drug use so that non-compliant patients can be encouraged to perform better have become standard."^v The proven benefit we've seen in drug development can benefit patients in their day-to-day care as well. Successful implementation of feedback that drives adherence in clinical practice will require interventions on multiple levels, involving healthcare providers, patients, the healthcare system, and may also require the development of new policies concerning access to patient's adherence data.

References:

ⁱ Duhigg, Charles. *The Power Of Habit: Why We Do What We Do In Life And Business*. New York: Random House, 2012. Print.

ⁱⁱ Identification and Assessment of Adherence-Enhancing Interventions in Studies Assessing Medication Adherence Through Electronically Compiled Drug Dosing Histories: A Systematic Literature Review and Meta-Analysis. Demonceau et al, *Drugs*, 2013, 73(6) 545-62.

ⁱⁱⁱ Successful Projection of the Time Course of Drug Concentration in Plasma During a 1-Year Period from Electronically Compiled Dosing-Time Data Used as Input to Individually Parametrized Pharmacokinetic Models. Vrijens et al., 2005, *J Clin Pharmacology*, 45(4): 461-7.

^{iv} *Methods for Measuring, Enhancing, and Accounting for Medication Adherence in Clinical Trials*. Vrijens, Urquhart, *Clin Pharmacol Ther*, 2014.

^v <http://www.fda.gov/DrugsGuidanceComplianceRegulatoryInformation/Guidances/default.htm>. Dec 2012

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SPECIFIC REQUIREMENTS

Author: Prof. Dr. Felix Ecker

SENIOR FRIENDLY PACKAGING

What are the special requirements?

As the number of 'silver-agers' continues to grow, complaints about non-senior-friendly packaging are also increasing. Thinking therefore about the special needs of seniors, there are a number of factors which would significantly improve a packaging concept. The list starts with force related issues, continues with vision dependent factors and concludes with cognitive challenges. But why are we talking about senior-friendly packaging and not about easy-to-open packaging? Are our fellow citizens with a long life experience really different from any other patient?

Nowadays, people not only enjoy a higher life expectancy, but they also expect better health and higher activity in later years. Is there really such a big difference between the average adult and our 65+ consumers or patient groups? What is clear is that there is a growing group of patients and consumers who have limited capabilities and consequently need special packaging.

We encourage everybody who is entrusted with the design and development of packaging to use their good sound judgment. Will your wife, husband, brother or mother face a challenge to open the product? Your customers will love you for it!

CHILD RESISTANT PACKAGING

Legislative requirements do exist for pharmaceutical pack labelling to assist in the prevention of accidental access to contents by children, including warnings such as 'keep out of the reach and sight of children', but this alone is not enough to prevent infant access to potentially dangerous medications.

Few countries have clear and concise laws on this topic outside of North America. In the US, Consumer Product Safety Commission regulation '16 CFR, part 1700' sets out rigorous requirements for packs wanting to claim child resistance as approved by the FDA. The US test involves seeing if young children can access a pack's contents initially by themselves and then again after being shown by an adult how to open the pack. The majority of packs in the US market are marketed in bottle type packaging as these are easy to safeguard and gain child resistant status. Few oral solid dose packs are presented in blister format, which is the opposite of the position elsewhere, as little or patchy legislation exists.

When considering the packaging for medicines, it is important to consider the environment that the medicine will be used in – is there a significant risk of infants accessing the drug? Another important consideration is to ensure that elderly patients, some with restricted mobility or eyesight issues, can access the medication too. A little thought in the early stages of pack design can really help this balance.

OVERALL CONCLUSIONS



Pharmaceutical design for patient friendly packs should be relatively straightforward to achieve. Even taking into account the product protection, regulatory compliance and manufacturing aspects, there is still significant scope to build in packaging features that can greatly help the patient to comply with the required dosing regimen and remain compliant throughout the entire dosing period.

There is still significant scope to build in packaging features that can greatly help the patient to comply with the required dosing regimen

Always consider designing/building your pack with the patient in mind, and in particular the following aspects:

- *Portability of medicine packs*
- *Ease of access to contents*
- *Reminder aids*
- *Discretion to allow private dosing*
- *Robustness of pack during use*
- *Intuitive use for the user*
- *Clear instructions!*

For more information about HCPC Europe, including case studies, resources, membership information and contact details, visit www.hcpc-europe.org

PHILL MARLEY

Packaging Intelligence Manager, AstraZeneca

Phill is a knowledgeable packaging specialist, with a passion for pharmaceutical manufacture and 29 years experience in the industry. He is a strong advocate for patient friendly packaging within the pharma industry. He has worked in many areas within AstraZeneca and currently has a global role as Packaging Intelligence Manager, monitoring, assessing and triggering the company's response to emerging legislation on serialisation. Phill is Chair of the Healthcare Compliance Packaging Council of Europe and a member of the EPFIA Packaging Technology and e-PIL teams.

JAN GEISSLER

Director, European Patients Academy on Therapeutic Innovation

Jan Geissler is Director of the European Patients Academy on Therapeutic Innovation. He is also founder and managing director of Patvocates, acting as an independent consultant in cancer policy, patient advocacy and social media. Being a leukaemia survivor who participated in various clinical trials himself, Jan founded the online patient community Leukämie-Online/LeukaNET in 2002. In 2003, he co-founded the European Cancer Patient Coalition (a European umbrella association of more than 300 cancer patient groups) and became its first full time director 2008. Jan also co-founded the CML Advocates Network which connects more than 70 leukaemia patient groups from more than 60 countries.

PROF. BERNARD VRIJENS

Chief Science Officer, MWV Healthcare Associate and Professor of Biostatistics University of Liège, Belgium

Dr. Vrijens is a co-author of two book chapters, over 60 peer-reviewed scientific papers, and named as inventor on two patents. He is a founding member and managing director of the European Society for Patient Adherence, Compliance, and Persistence, and an active member of several EU- and US-funded collaborative projects around the theme of adherence to medications.

TASSILO KORAB MSC

Executive Director HCPC Europe

Tassilo Korab has been in the packaging industry for more than 30 years. He holds an MSc in Healthcare Economics and has written several publications on patient compliance, standards and regulations for child resistant packaging and the war against counterfeits. He is Managing Director of TKM Handelsg.m.b.H. in Vienna and was one of the co-founders of HCPC Europe, serving as executive director from 2005 to 2015.

PROF. PRZEMYSŁAW KARDAS MD, PHD

Head of First Department of Family Medicine, Medical University of Lodz, Poland

Professor Kardas focuses on patient adherence to medication, doctor-patient communication and the management of chronic conditions in outpatient settings. He is the author of a number of peer-reviewed scientific publications and conference presentations, as well as two monographs. He is a member of several editorial boards and a reviewer for a number of medical journals. He also serves as an expert to the European Commission on Public Health and is involved in numerous international research collaborations.

DR. THOMAS DRIES

Market Development Manager Honeywell

Dr. Thomas Dries is a member of Honeywell's Global Healthcare & Packaging Team. For more than 24 years he has been engaged in the development and marketing of polymer films for the packaging of food, non-food and medicines. Thomas shares a passion for pack designs of medicines that help create positive responses from users and good treatment outcomes at the same time. Thomas is co-founder of HCPC Europe and was the organization's chairman from 2003 - 2011.

PROF. DR. FELIX ECKER

Hochschule Fulda, University of Applied Sciences & Geriatric Medicine Society

Prof. Dr. Felix Ecker is Professor for Pharmaceutical Technology and Packaging Science in the Department of Food Processing Technology at the Hochschule Fulda, University of Applied Sciences in Germany. A licensed pharmacist, Professor Ecker previously worked for Bayer Healthcare in Germany, USA, Mexico and China.

DR. KAREL VAN DER WAARDE

Graphic Design - Research, Elewijt (Belgium)

Karel van der Waarde studied graphic design in the Netherlands (The Design Academy, Eindhoven) and in the UK (De Montfort University, Leicester and the University of Reading). In 1995, he started a design/research consultancy in Belgium specializing in the testing of medical information design. His company develops patient information leaflets, instructions, forms, protocols and the information architecture for websites.

ANDREW LOVE MENG CENG MBA

VP Capability Development, Be4ward Ltd

Andrew is currently Vice President Capability Development at Be4ward Ltd, assisting a number of pharmaceutical clients with packaging management related engagements. Prior to this, Andrew led GlaxoSmithkline's (GSK) global packaging design operations until 2009, where he was responsible for the transformation of their capabilities into a best in class operation.

DIPL. ING. THOMAS SEFRIN M.SC.

Global Leader Packaging Design Management, Novartis Pharma AG

Thomas' passion is packaging design and technology. In the last 15 years he has worked in various roles in Packaging Development and Management in both FMCG and pharmaceuticals. His focus is the design of packaging solutions that make a difference in people's life. In his current role he is developing and overseeing the global design processes at Novartis.

STEFANIE MEIER B.ENG. & M.SC.

Global Packaging Design Manager, Novartis Pharma AG

Stefanie has chosen a specialized career in packaging technology, packaging design and marketing. She started her professional life with Novartis in 2012 focusing on need-oriented packaging design for solid oral prescription drugs. In her current role as Global Packaging Design Manager at Novartis Pharmaceuticals she promotes holistic and balanced packaging solutions for all stakeholders - from patient needs to manufacturing requirements.

NABEELA BUTT BSC, MTOPRA

Abbot Pharmaceuticals

Ms Butt is a pharmaceutical professional with over 15 years experience in the industry ranging from packaging development, artwork management and International, EU, UK and Global Regulatory Affairs. Ms Butt is originally from Kenya but was raised in London.

