Use As Directed

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Introduction

The growing concern within the pharmaceutical industry is the role that packaging plays within the doctor-patient cycle. Prescription medications are administered to the patient and it is assumed that the correct type, dosage, and amount will be given. According to the Food and Drug Administration (FDA), 1.3 million people are unintentionally harmed every year in hospitals and in-patient healthcare facilities because of improper medication use and medical device failures. Moreover, the FDA states that prescription drug packages and labels that are misunderstood by the caregiver cause many of these problems (Mayberry, 1998). With the increasing number of prescription drugs and medications being used by consumers today, special attention must be paid to the packaging and its role in terms of child-resistance, senior-friendliness, and its overall convenience.

Safety Concerns of Current Drug Packaging

Packaging is expected to help reduce such medication errors. New senior-friendly packaging should help reduce the one million yearly calls about ingestions to poison control centers, 130,000 hospital emergency room treatments of poisoning, and 50 poisoning deaths to young children (CPSC, n.pag). The Harvard School of Public Health cited research indicating that as many as 10 percent of all patients experience an adverse drug event during hospital treatment, even though only 0.2 percent of these events are reported. This statement is based on quantification efforts undertaken by Harvard to objectively measure the number of adverse drug events that have occurred within the University's hospital system (Mayberry, 1998).

In recent years, both the healthcare industry and the general public have become more aware that poor patient compliance leads to failed medication regimens. There also seems to be an increased awareness of how labeling and packaging, especially unit-dose packaging such as blister cards, can help patients with compliance. One hospital reported a 70 percent decrease in errors when its pharmacy switched to bar-coded, unit-dose packaging (Swain, August 2000). Along with the issues of medical errors, other dilemmas regarding pharmaceutical packaging arose, including patient compliance to their regimens. Bill Arden, marketing manager at TL Systems Corporation Bosch Group stated, "Patient noncompliance in a drug regime is one of the biggest problems a doctor can have and is becoming bigger as the population ages" (Erickson, 1998). A report done by the Institute of Medicine indicated that an improved package could help. Unit-dose packaging is particularly suited for this task.

This type of packaging has the ability to not only protect children and be potentially senior-friendly, but it can also be used to inform the user. Doctors can write all of the regulations that they want, but it is in the patient's hands when the patient takes the medicine home. The use of unit-dose packaging can prevent and substantially reduce the number of poisoning incidents that occur each year.

Medication errors are also associated with poor product packaging design. Severe toxicity and death due to overdoses of certain drugs usually appear to be the same as other less toxic drugs on the packaging, but in fact they are not (Proulx, 2000). Manufacturers should take precautions during the design process to prevent such tragic mistakes as the overdoses, considering there are at least 29 cases per year (Proulx, 2000).

To combat this issue of brand recognition, typeface is being considered to enhance distinctive portions of look-alike drug names on look-alike packaging. Hopefully, the introduction of unit-dose packaging into the diverse group of prescription medications will have a positive effect on the industry.

Daily, physicians, nurses, and pharmacists base medical decisions on information provided by a drug product's labeling and packaging. Unfortunately, poor labeling and packaging have been linked all too often to possible cases of medication errors (Proulx, 2000). Unit-dose packaging can be considered a solution to the safety concerns that arise when prescription medications are involved. Only when the industry, government, and consumers begin to carry out their individual responsibilities, can we effectively reduce the number of ingestions and poisonings that occur each year in the U.S. When one in ten patients is found to be experiencing adverse drug events and credible sources have identified potential solutions, immediate action should be taken (Mayberry, 1998).

Regulations and Blister Packaging

In the debate concerning efforts to encourage the use of unit-dose packaging, there are several regulations and market developments that are pushing many manufacturers to pursue new designs.

Unlike bottled medication, blister packaging is designed to keep each dose fresh until needed. To ensure that blisters actually do protect their contents from moisture, humidity, and other environmental hazards, drug packagers need to subject the packages to a series of environmental challenges known as product stability tests.

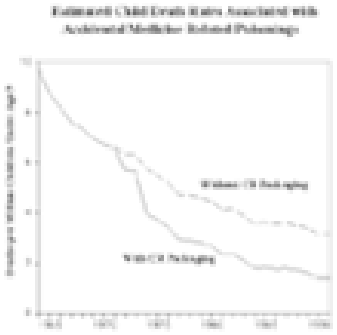
The code administered by the FDA, section 211.166 of title 21, mandates the performance of stability testing. The results of this testing shall be used in determining appropriate storage conditions and expiration dates (Allen, 1999).

In the latest developments regarding stability testing, FDA guidelines changed the accelerated stability test from 3 months at 38 degrees C, 90 percent RH to 6 months at 40 degrees C, 75 percent RH (Beagley, 1998). Such changes in testing protocols will make new packaging designs more challenging. Engineers must consider using new materials that will increase the barrier

properties and comply with the modifications made to the Poison Prevention Act of 1970.

The Poison Prevention Packaging Act (PPPA) was ratified recently to protect young children from accidental ingestion of harmful substances. As seen in Figure 1, the passage of the PPPA requires the use of child-resistant packaging, the commission estimated that over 700 children's lives have been saved from accidental poisonings by prescription drugs and aspirin alone (CPSC, n.pag).

Figure 1: Child Death Rates



Some children however, continued to be poisoned. Many adults who have had difficulty opening bottled packages defeated the purpose by throwing the caps away. Transferring hazardous substances into other non child-resistant packaging has been another problem. Under the original PPPA regulations, packages were tested with panels of children less than 5 years of age to ensure child-resistant packaging was difficult to open. Manufacturers also tested panels of individuals 18 to 45 years of age to ensure that adults could use the packaging as well.

Unfortunately, despite this testing, many adults, including the elderly, still had trouble opening the packaging. In June 1995, the U.S. Consumer Product Safety Commission (CPSC) voted unanimously to issue a final rule modifying the child-resistant packaging test protocols of the PPPA (CPSC, n.pag). These changes revised the testing methods, which made packaging senior-friendly and easy to open while maintaining their child-resistance. The CPSC's decision changed the make-up of the test panels, from individuals 18 to 45 years of age to individuals 50 to 70 years of age. This gave a better understanding of the abilities of normal adults using child-resistant packaging.

Approximately 20 percent of the children being poisoned by pharmaceuticals were poisoned by their grandparent's medicine (Beagley, 1998). Such statistics show that the older adult populations were not effectively opening and closing their prescription medicines, which resulted in the Poison Prevention Act to ensure the safety of children. The modification of the law will force most drug manufacturers to look for new, innovative packaging to accommodate the physical demands of their sensitive products. Unit-dose packaging provides a positive answer to the pending dilemma of adhering to regulations while preserving the integrity of sensitive medical products.

The CPSC revised its regulations with intent to protect children from accidental poisonings, not to disrupt the pharmaceutical industry. Fortunately, the industry has shown strong support by taking a common sense approach to packaging designs and testing.

The CPSC and the industry cooperated to prevent future deaths and poisonings of children. Hopefully, this will reduce the risk of child poisoning from medicines transferred to non child-resistant packaging or from packaging where the tops are left off. When the CPSC revised its protocol, requiring that drug packages be senior- friendly as well as child-resistant, blister packaging designers were faced with a challenge.

The Role of Unit-Dose Packaging in Pharmaceuticals

Many manufacturers, who had previously sealed their packages tightly to keep children out, had not taken senior-friendliness into account. Some blister packages will continue to be made that way, because the protocol allows a unit-dose package to pass the senior-friendliness test by the use of opening it with scissors (Swain, February 2000). Blister manufactures must look for innovative ways to design new packaging that complies with child-resistance and senior-friendly regulations for many reasons. Simply calling for the use for scissors will not work for a growing number of new drugs that must be packaged in blisters because of their high toxicity levels. In some cases, if a senior citizen skips a dose or stops taking the drug because of frustration over the packaging, it could result in a life or death situation. The phrase "open with scissors" or "cut here" enables the packages to be opened by a senior test panel (Swain, February 2000). However, it cannot recommend using a scissors icon on the package showing where to cut. A child will recognize that icon, get the scissors, and be able to get into the blister. When considering the use of scissors to open blister and unit-dose packaging manufacturer should "say it," but don't "show it" (Swain, February 2000).

The danger of introducing child safety precautions may compromise usability of packs with less dexterous people. However, the latest change in safety standards provides a huge opportunity to rethink medicine packaging designs. Historically, when designers have achieved child-resistance in their packaging designs, it had commonly come at the expense of senior-friendliness, but now there are several options to overcome these conflicting requirements. As a result of the change in packaging protocols, there is a new blister package design whose opening features use an entirely different set of parameters. Instead of relying on force, which troubles seniors, to open the package, these designs accommodate certain abilities that seniors possess and children do not. For example, reading comprehension, the ability to follow several numbered tasks, and ability. The task of designing a package that focuses on cognitive ability to open rather than strength is to limit the number of movements to simplify opening. Designers must limit to three or fewer movements until the product can be reached, otherwise, people may not remember how to open it (Swain, February 2000). The first generation of child-resistant blisters has been creative, but also labor intensive. An example of a newer unit-dose package is the Dosepak‰ from Mead Westvaco Corp., Some of these

solutions are incredibly expensive, particularly if you are only doing a small run of 3,000 to 4,000 packs, because of set up costs. However, the company has sold 2.6 million Dosepack units since the CPSC regulations went into effect (Polin, 2002). One-third of the orders they received have been for trials requiring 4,000 units or less (Polin, 2002). The new Dosepak contains three main design elements: an outer carton, fold over inner blister card, and a unique locking feature.

Figure 2: Dosepak

It features an inner blister sealed to an outer paperboard carton. This provides child-resistance through a locking mechanism that children don't realize exists. Once the locking mechanism is released and the package is opened, the individual blisters make it easy for seniors to open. The carton also has a tear-resistant laminate, because ripping is the most common way children try to get into blister packaging. In addition, Mead Westvaco's category manager, Michael Hubble, mentions that the carton provides ample room for compliance-related information, and the paperboard is hard to dispose of because it is attached to the blister, meaning that the child-resistant feature and the labeling always remain (Packaging Digest, July 2001).

"The focus of these concepts is on cognitive ability," said Patrick H. Dent, technical coordinator of pharmaceutical and healthcare markets for Reynolds's Global Packaging Group. "Many seniors don't have the dexterity or strength to open conventional packages" (Swain, 2001).

Dosepak offers other advantages as well. For pharmaceutical manufacturers, Dosepak can be used in clinical trials, where the toxicity of a drug may still be unknown, and then commercialized simply by changing its graphics. Dosepak helps consumers to maximize effectiveness and follow regimens, such as taking medication with meals or at certain times of the day, by allowing manufacturers to incorporate graphics, icons, and other instructions on the interior and exterior of the package.

Another option that Mead Westvaco offers in regards to unit-dose packaging is the Surepak. Surepak consists of a tear-resistant paperboard cover which is wrapped around a high-strength plastic frame. A proprietary locking mechanism on one side of the frame snaps closed over the cover and holds it into place. When the lock is disengaged and the cover lifted, an inner blister card attached to the underside of the cover lifts it. When the cover is closed, the blister card rests back inside the frame, leaving space for CD-ROMS, product brochures, safety and compliance guidelines, and other product information

(Design Week, 2002). According to Mead Westvaco, Surepak has achieved a child-resistance at the F=1 level, the safest U.S. government rating for medical packaging. That rating also means any inner blister card used with the new package will carry the F=1 level as well (Gale Group, 2003). An F=1 rating indicates that in a test group of 50 children, only one child was able to open the package within a five minute window. After several redesigns, the package was able to pass the CPSC testing protocol without any children gaining access to any pills, so it can be used for the most toxic drugs (Gale Group, 2003).

In addition to prescription drugs, Surepak is said to be suitable for nutritional supplements and other healthcare products. The senior-friendly inner blister card extends product shelf life and offers space to guide consumers through the correct dosage regimens. These new packages can be used in semi-automatic or high speed filling environments and can be customized in any size or color. Manufacturers can still make the switch to unit-dose packaging while not compromising their manufacturing processes, this makes Surepak more desirable. Blisters promote compliance, more so than bottles, by presenting a means by which a patient or subject will know what dose was taken last and/or what dose was missed.

A 1991 study found that elderly patients using unit-dose calendar packaging were more likely to comply with their regimens than those using bottles or other noncalendar packs. The users of calendar packages led in compliance rates by 86.7 to 66.7 percent (Swain, 2001).

Another reason for the increased interest in designing compliance packages is the transition of certain drugs from multi-doses per day to one dose per day or even one dose per week. If a dose is missed there is a greater effect, therefore compliance becomes more critical.

Perhaps the most significant advantage that unit-dose packaging and blisters have is their set of clear directions, telling when one should take the medication. This advantage enables the consumer to be well informed regarding dosage, frequency, and product warnings.

Industry Outlook

The use of unit-dose packaging is rapidly expanding in the U.S. There has been a growth in unit-dose packaging for the healthcare providers, specifically in hospitals, prisons, and nursing homes (Erickson, 1998). What seems to attract these providers to this type of packaging are issues of self-medication and positive identification of the product. When considering the issues of unit-dose packaging and its growth within the industry, one must realize that the amount of people using medications has increased as well as the diversity of medications. Industry insiders and observers generally agree that the use of blisters, including unit-dose packaging, will grow by at least 12 percent per year (Erickson, 1998). The greatest advances in market share are projected to come from blister packages, which are predicted to reach $1.045 billion in 2004 (Swain, August 2000). These numbers are very promising when compared to other various types of packaging used in the pharmaceutical industry. The projected growth of blisters and unit-dose packaging shows a wider industry

acceptance of the packaging design and the willingness to protect children while not compromising ease of use.

Figure 3: Pharmaceutical Packaging Demand in Millions ($)

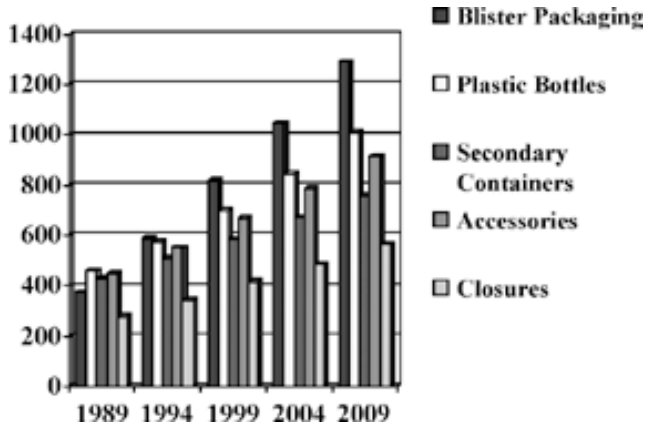
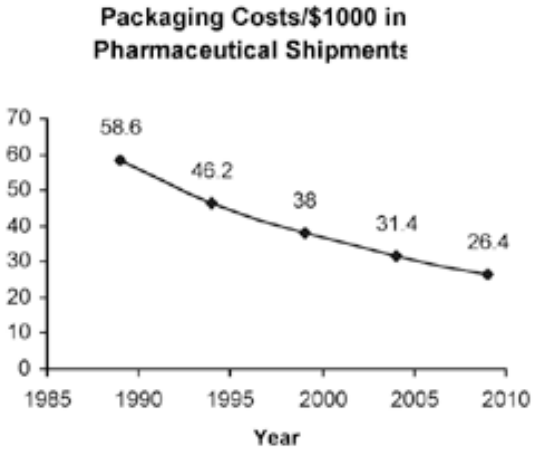


Figure 3 compares the various types of containers used in the pharmaceutical industry, and specifically outlines the growth of blister packaging compared to the growth of other drug packaging. Historically, the growth of blister packaging has been steady. Now that the use of unit-dose packaging has been projected to gain more industry acceptance, that number is expected to rise to approximately 12 percent per year.

Figure 4: Shipment Costs



Along with an increase in blister sales, Figure 4 shows the cost of packaging per pharmaceutical shipment is dropping significantly, according to the Freedonia study. In 1989, drug companies spent $58.60 on packaging for every $1000 in pharmaceutical shipments. In 1999 that dropped to $38.00; it is expected to drop further to $31.40 in 2004 and $26.40 in 2009, indicating that drug companies are as serious about keeping packaging costs down (Swain, August 2000).

Two key points regarding the industry acceptance of unit-dose packaging are the initial setup costs and the concerns as to whether the new packaging designs will be profitable. Warner-Lambert, the producer of the cholesterol-lowering drug Lipitor, can be used as an example. According to Thomas McMurray, Warner-Lambert's Director of Packaging Technology, in 2000 alone the company lost nearly one billion dollars in sales. The majority of those losses were due to patient non-compliance. McMurray explained that in the next year, patient termination of the drug based on non-compliance may reduce the drugs revenue by an additional ten billion dollars nationwide (Allen, 2000).

Unit-dose packaging, however, may be able to turn such losses into gains. "Sixty percent of patients stop taking Lipitor after six months, and such non-compliance is common with other drugs," said McMurray.

If drugs were to be packaged in unit-dose packaging such as blister packs, patients would have a daily reminder and record of their regimens, and therefore a greater chance of adhering to them (Allen, 2000).

However, the same manufacturers who fear non-compliance may shy away at the thought of placing all of their drugs into unit-dose packaging. Material, equipment, tooling, and labor costs associated with unit-dose blister packaging are often high enough to deter companies that are accustomed to using bottles.

Drug makers may be able to increase their product value enough so that volume increases actually lead to a "break even" point in costs between bottles and blisters (Allen, 2000). The key is to find the knee in the price/volume curve, which is the point at which the cost floor of high-volume production is in sight. At the beginning of the curve, manufacturers must pay for development, tooling, and production costs, whereas at the end, manufacturers only pay for materials. The point is, to be able to reach the end of this price/volume curve; manufacturers must get volume up to get cost down. The key to increased volume is to convince patients, practitioners, and buyers of the value of unit-dose packaging (Allen, 2000). If drug manufacturers can convince users of the value of packaging that encourages regimen compliance, more manufacturers may be able to afford and profit from a packaging technology that could help save lives, while not compromising ease of use.

Conclusion

The unique characteristics of unit-dose packaging offer a positive solution to the issues that the medical and pharmaceutical industries face. The new packaging allows consumers to safely follow their drug regimen through clear labeling and instructions, ease of use, all the while providing the relief of child-resistance. Unit-dose packaging has increasing industry acceptance and the potential to dominate the pharmaceutical market. With advances in material and packaging designs, unit-dose packaging will continue to grow in the medical market.

Hopefully, with the increased popularity of the packaging, there is a decrease in accidental poisonings, medical errors, and deaths. Unit-dose packaging can be considered a new technology in the market, with the potential for

great success. Only those companies ahead of the game will reap the benefits.

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