

## Review Article

## Recent Trends in Pharmaceutical Packaging: A Review

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### ABSTRACT

Packaging played a significant role in the pharmaceutical field as it maintains the integrity of product by many ways, like providing presentation, protection, identification, information. Containment, convenience and compliance for a product during storage, carriage, display and until the product is consumed. This article reviewing the various aspects of packaging like materials used for packaging, types of packaging as well as recent trends of pharmaceutical packaging in pharmaceutical market.

**Keywords:** Packaging, Glass, Plastic, Recent trends.

### INTRODUCTION

Packaging can be defined as an economical means of providing presentation, protection, identification information, containment, convenience and compliance for a product during storage, carriage, display and until the product is consumed. Packaging must provide protection against climatic conditions biological, physical and chemical hazards and must be economical. The package must ensure adequate stability of the product throughout the shelf life.<sup>1</sup>The external image of the package must not only compliment product confidence, but provide clear and concise product identification and other features included are:

- Package should provide adequate information related to the contents including legal requirements, route of administration, storage conditions, batch number, expiry date, manufactures name and address and product license number.
- Package should assist in patient compliance.
- Package should preferably have an aesthetically acceptable design.

The primary packaging consist of those packaging components which have a direct contact with the product (i.e. bottle, cap, cap liner, label etc). The main functions of the primary package are to contain and to restrict any chemical,

climatic or biological or occasionally mechanical hazards that may cause or lead to product deterioration. Packaging must also function as a means of drug administrations. The packaging external to the primary package is known as the secondary packaging. The secondary packaging mainly provides the additional physical protection necessary to endure the safe warehousing and for refill packaging.(Table1)

### Types of container used as primary packaging for liquid orals are:

**Single dose containers** hold the product that are intended for single use like glass and ampoule.

**Multi-dose containers** hold a quantity of the material that will be used as two or more doses. Like multiple doses vial plastic tablet bottle.

**Well-closed containers** protect the product from contamination with unwanted foreign materials and form loss of contents during use.

**Airtight containers** are impermeable to solids, liquids and gases during normal storage and use. If the container is to be opened on more than one occasion it must remain airtight after re closure.

**Light – resistant container** protect the contents from the effect of radiation at a wave length between 290nm and 150nm.

**For solid dosage forms**

**Tamper – evident containers** are closed containers fitted with a device that irreversibly indicates if the container has been opened.

**Strip packages** have at least one sealed pocket of material with each pocket containing a single dose of the product. The package is made of two layers of film or laminate material. The nature and level of protection which is required by the contained product will affect the composition of these layers.

**Blister packages** are composed of a base layer, with cavities called blisters which contain the pharmaceutical product, and a lid. This lid is sealed to the base layer by heat, pressure or both. They are more rigid than strip packages and are not used for powders or semi-solids. In tropical areas blister packages with an additional aluminium membrane is used which provide greater protection against high humidity.

**Child Resistant Containers**, commonly referred to as CRC's, are designed to prevent the child accessing the potentially hazardous product.<sup>2</sup>

**Containers for semisolid and pressurized products:** Semi solid dosage forms like ointments, creams etc. are packed in metallic collapsible tubes. Plastic containers are also used for the packaging of creams. Pressurized packages expel the product through a valve. The pressure exerted for the expulsion of the product is an important consideration while selecting the packaging for any products.

**Factor influencing the choice of package:** It is essential to have a survey about the market, the distribution system, manufacturing facilities and other considerations before selecting the packaging material.

**The product:** The physical and chemical characteristics of the drug entity, the excipients, the formulation, route of

deterioration of the product, type of patient (baby, child, teenager, adult, elderly, infants etc.) must be considered while dealing with the pharmaceutical product.

**The market:** The channel of sale should be considered, i.e. where, when, how and by whom it is to be used or administered (e.g. doctor, dentist, nurse, patients etc), whether for home trade and/ or export. The quantity per package and follow up sale must all be carefully considered during package design and selection.

**The distribution system:** The distribution system should be carefully monitored, e.g. conventional wholesale/ retail outlet or direct or selective outlets.

**Manufacturing facilities:** The stability of the manufacturing facilities should be considered due to new package, increased sale, improvements in Good Manufacturing Practice, revised product, new product etc.

**Function of packaging**

**Protective function:** Protective function of packaging essentially involves protecting the contents from the environment and vice versa. The inward protective function is intended to ensure full retention of the utility value of the packaged goods. In addition packaging must essentially be able to withstand the many different static and dynamic forces to which it is subjected during transport, handling and storage operations. The goods frequently also require protection from climatic conditions, such as temperature, humidity etc.

**Storage function:** The materials used for packaging should be stored properly so as to preserve the quality of the material both before packaging and once the package contents have been used.

**Loading and transport functions** Packaging should therefore be designed to be easily handled and to permit space-saving storage and stowage. The shape and strength of packages should be such that they may not only be stowed side by

side leaving virtually no voids but may also stowed safely one above the other.

### Properties of packaging materials

**Mechanical Properties:** The materials used should possess sufficient mechanical strength to withstand while handling, filling, closing and processing. Typical care is needed during transport, storage and also at the time of usage by the consumer especially in case of glass containers.

### Physical properties

- The packaging must have a suitable size, thus, rubber may presents problems if it perishes.
- The material must protect from light if necessary, that is, it must be ultraviolet absorbent.
- The container must not absorb substances from the products; e.g. absorption of water from creams in to cardboard box.

### Chemical properties

- The product should not react with the container or closure, as might happen if alkaline substances are placed in aluminium containers.
- The container or closure must not yield substances to the product; for example, alkali from glass, plasticizers from plastics etc.

### Biological properties

The material of the container must be able to withstand attack by insects if this hazard is likely to be encountered. The packing should not support mould growth.

### Hazards encountered by package

#### Mechanical hazards

**Shock or impact damage:** Damage due to shock is usually caused by rough handling, during transport etc. Cushioning can be provided and a warning label may be useful. Restriction of movement and more careful handling should be made.

#### Compression

Fragile items may be broken, or collapsible articles crushed by compression, the usual procedure then

being to protect with a rigid outer package. Top pressure or loading can distort inside.

### Vibration

Vibration consists of two variables-frequency and amplitude. Considerable vibration may occur during transport, especially with exported items. Damage may be external, such as the 'scuffing' of labels, but some products may be affected like the cracking of emulsions, abrasion of tablets, or segregation of mixed powders.

**Environmental hazards:** Environmental conditions encountered by the package are likely to vary considerably, especially in articles for export to the tropical areas.

**Temperature:** Extreme conditions may cause deterioration, low temperatures leading to aqueous solutions freezing and, hence, to fracture of containers.

**Moisture:** Moisture as liquid or water vapour may cause physical changes (e.g. color fading, softening, hardening etc.) or chemical changes (hydrolysis, oxidation, effervescence etc.).

**Pressure:** Decrease in pressure, as in mountainous regions or during flight in non-pressurized transport aircraft, may cause thin containers to burst or strip packs to inflate.

**Biological hazards:** The packaging materials must be reasonably clean initially and when put together to form a finished package and restrict any further contamination as much as possible. In the case of sterile products the package and its closure must maintain a 100% effective seal against microbiological contaminants like bacteria, moulds and yeasts.

**Chemical Hazards:** The main risk of chemical hazard is due to interaction or incompatibility between the product and package. These may be associated with interaction or contamination, covering migration, absorption, adsorption, extraction, corrosion, etc.

### **Packaging materials used in different formulations**

**Paper and board:**The use of paperboard materials remains a significant part of pharmaceutical packaging in spite of the facts that paper is rarely used on its own for a primary package. Cartons are used for a high percentage of pharmaceutical products for a number of reasons, increasing display area, providing better display of stock items and the collating of leaflets which would otherwise be difficult to attach to many containers. Cartons also provide physical protection especially to items such as metal collapsible tubes. Carton therefore tend to be a traditional of pharmaceutical packaging.

**Rubber based components:** Rubber components may be made from either natural or synthetic sources. Natural rubber has got good resealing, fragmentation and coring when compared to synthetic rubber; but is poor in respect to ageing and chances of moisture and gas permeation and the absorption of preservative systems is more. Most rubber formulation are relatively complex and may contain one or more of the vulcanizing agents, accelerators, fillers, activators, pigments, antioxidants, lubricants, softeners or waxes<sup>3</sup>.

**Tamper resistant packaging:**The requirement for tamper –resistant packaging is now one of the major consideration in the development of packaging for pharmaceutical products As defined by the FDA "a tamper –resistant package is one having an indicator or barrier to entry which, if breached or trussing ,can reasonably be expected to provide visible evidence to consumers that tampering has occurred tamper –resistant packaging may involve immediate – container /closure systems or secondary – container /carton systems or any combination thereof intended to provide a visual indication of package integrity when handled in a reasonable manner during manufacture ,distribution ,and retail display<sup>4</sup>.

The following package configuration have been identified by the FDA as examples of

packaging systems that are capable of meeting the requirements of tamper-resistant packaging as defined by FDA regulation

1. Filmwrappers
2. Blisterpackage
3. Strippackage
4. Bubblepack
5. Shrinksealandbands
6. Foilpaperorplasticpouches
7. Bottleseals
8. Tapeseals
9. Sealedtubes
10. Aerosolcontainers
11. Sealed cartoon

**Film wrapper:**Film wrapping has been used extensively over the years for products requiring package integrity or environmental protection. Film wrapping can be accomplished in several ways and varies in configuration with packaging equipment.

**Fin seal wrapper:**The seal are formed by crimping the film together and sealing together the two inside surface of the film, producing a "fin" seal Since the seals are formed by compressing the material between two heater bars rather than sealing against the package. When more consistent and greater sealing pressure is applied, better seal integrity can be accomplished .For this reason, fin sealing has primarily been used when protective packaging is critical . Since the surface of the heat seal dose not come in contact with the heated sealing bars on the packaging equipment, much more tenacious heat sealants such as polyethylene can be used.

**Shrink Wrapper:** Film over wrapping can also be accomplished with the use of a shrink wrapper .The shrink wrap concept involves the packaging of a product in a thermoplastic film that been stretched and oriented during its manufacture and that has the property of reverting back to its un-stretched dimension once the molecular structure is "unfrozen " by the application of heat.

**Blister Package:** This packaging mode has been used extensively for pharmaceutical packaging for several good reasons. It is a packaging configuration capable of providing excellent environmental protection, coupled with an esthetically pleasing and efficacious appearance.

**Strip Package:** A strip package is a form of unit dose packaging that is commonly used for the packaging of tablets and capsules. A strip package is formed by feeding two webs of a heat-sealable flexible film through either a heated crimping roller or a heated reciprocating plate. The product is dropped into the pocket formed prior to forming the final set of seals

**Bubble Pack:** The bubble pack can be made in several ways but is usually formed by sandwiching the product between a thermoformable, extensible, or heat-shrinkable plastic film and a rigid backing material.

**Shrink Banding:** The shrink band concept makes use of the heat-shrinking characteristics of a stretch-oriented polymer, usually PVC. The heat-shrinkable polymer is manufactured as an extruded, oriented tube in a diameter slightly larger than the cap and neck ring of the bottle to be sealed. The heat-shrinkable material is supplied to the bottler as a printed, collapsed tube, either pre-cut to a specified length or in roll form for an automated operation.

**Foil Paper or Plastic Pouches:** The flexible pouch is a packaging concept capable of providing not only a package that is tamper-resistant, but also by the proper selection of material, a package with a high degree of environmental protection. A flexible pouch is usually formed during the product filling operation by either vertical or horizontal forming, filling and sealing (f/f/s) equipment.

**Bottle Seals:** A bottle may be made tamper-resistant by bonding an inner seal to the rim of the bottle in such a way that

access to the product can only be attained by irreparably destroying the seal. Various inner seal compositions may be used, but the structures most frequently encountered are glassine and foil laminations

**Tape Seals:** Tape sealing involves the application of a glued or pressure-sensitive tape or label around or over the closure of the package, which must be destroyed to gain access to the packaged product. The paper used most often is a high-density lightweight paper with poor tear strength.<sup>4</sup>

**FDA regulation:** Food and Drug Administration evaluates a drug and the agency must be firmly convinced that the package for a specific drug will preserve the drug's efficacy as well its purity, identity, strength and quality for its entire shelf life. Under the provisions of the Food and Drug Administration Act, however, no specifications or standards for containers or container closures are provided.<sup>5</sup> Under the Act, it is the responsibility of the manufacturer to prove the safety of a packaging material and to get approval before using it for any pharmaceutical product. The Food and Drug Administration does not approve containers as such, but only the materials used in the container are approved. A list of substances considered "Generally Recognised As Safe" (GRAS) has been published by the FDA. In the opinion of the qualified experts they are safe under specified conditions, assuming they are of good commercial quality. A material that is not included under GRAS or prior sanction, and is intended to be used with food, must be tested by the manufacturer, and the data must be submitted to the FDA.<sup>5</sup> The specific FDA regulation states that "containers, closures and other component parts of drug packages, to be suitable for their intended use, must not be reactive, additive or absorptive to an extent that the identity, strength, quality or purity of the drug will be affected." The packaging material must be approved for such use, along with the drug, before going to the market. The drug

manufacturer must include data on the container and package components in contact with the pharmaceutical product in its New Drug Application (NDA). If the FDA can determine that the drug is safe and effective, and that the package is suitable, it approves the drug and package. Once approved, however, the package may not be altered in any manner without prior FDA approval. In the case of plastics, most resin manufacturers maintain Master Files on their resins with the FDA. Upon request from the resin manufacturer, the FDA uses this file as a reference to support a New Drug Application that which a drug manufacturer files.<sup>6</sup>

### **RECENT TRENDS IN PHARMACEUTICAL PACKAGING IN INDUSTRY**

The pharmaceutical packaging market is constantly advancing and has experienced annual growth of at least five per cent per annum in the past few years. The market is now reckoned to be worth over \$20 billion a year. As with most other packaged goods pharmaceuticals need reliable and speedy packaging solutions that deliver a combination of product protection, quality, tamper evidence, patient comfort and security needs. Constant innovations in the pharmaceuticals themselves (such as prefilled syringes, blow fill seal vials, powder applications and others) also have a direct impact on the packaging. Traditionally, the majority of medicines (51%) have been taken orally by tablets or capsules, which are either packed in blister packs (very common in Europe and Asia) or fed into plastic pharmaceutical bottles (especially in the USA). Powders, pastilles and liquids also make up part of the oral medicine intake. However, other methods for taking medicines are now becoming more widely used. These include parenteral or intravenous (29%), inhalation (17%), and transdermal (3%) methods. Oral tablets themselves are also now available in a wide range of different shapes and sizes. These changes have made a big impact on the packaging industry and

there is an increasing need to provide tailored, individual packaging solutions, which guarantee the effectiveness of medicines. Due to degradation from environmental factors, such as light and humidity, there is often a direct link between packaging and a remedy's effectiveness. Packaging of oral medicines generally conforms to requirements for easy dispensing, child resistance but senior-friendliness, but packs must also be identifiable, functional and very often hermetically sealed. However, some innovations provide added benefits in one area but may not conform to the expected standards governing another. For instance, blister packs provide convenience and ensure hygiene. They are ideal for our fast-paced lifestyles and the need to take medication on the go and, as a result, there has been a large increase in their use. Indeed, blister packaging has provided the best worldwide growth among all pharmaceutical packaging products, with demand increasing 6.2 per cent annually to over \$4 billion in 2006. Advances in the packaging machines themselves has seen the incorporation of precise filling mechanisms, as the wrong dosage of a medicine could be life threatening. Gentle handling is also essential and packs should be hermetically sealed for higher product safety. A solution to achieve hermetically sealed packs for blister, blow-fill-seal pouches, vials and other products is to overwrap them into a horizontal flow wrap. These flow wraps consist of a foil laminate that is able to increase the shelf life of the product as well as to ensure 100% tightness. Some packaging needs are not driven by the need for hygiene, safety or traceability. The increased focus on marketing of pharmaceutical products will become even more important in the future and will drive factors such as the need for flexibility in terms of various pack types and sizes. Other needs are simply driven by costs as pharmaceutical manufacturers face increased cost pressures throughout the entire production and packaging process. As a result, packaging machines have to become more efficient and user friendly, offering

flexibility, easy operation, robustness, intelligence and protection from interference. It is a challenge to cover all aspects at once.

The ongoing globalization trend with extended competitive landscape in the pharmaceutical industry will lead to smaller batch sizes. If existing packaging equipment is used, this will have a negative effect on productivity, as older machines are often not designed for quick changeovers and flexibility. New packaging lines will have to offer high flexibility while maintaining production levels. World demand for pharmaceutical packaging is forecast to rise 5.5 percent annually through 2015. The developed countries of Western Europe, the US and Japan will account for over 70 percent of the amount, although China will provide faster growth opportunities. India and Brazil will also evolve into fast-growing markets. This study analyses the \$47.2 billion world drug packaging industry. It presents historical demand data for the years 2000, 2005 and 2010, and forecasts for 2015 and 2020 by raw material (e.g., plastic resins, paper and paperboard, glass, aluminium foil), product group (e.g., primary containers, closures, labels, secondary containers, prescription containers, accessories), world region and for 14 countries<sup>7</sup>. Strong growth in emerging markets such as India and China has contributed to an increase in revenue optimism. The packaging sector in India is growing considerably and is expected to increase over the next two years, due to the high demand from industry sectors such as food and beverage and pharmaceutical packaging. Moreover, the global market recovery will aid growth expectations as it will result in increased demand for packaging machinery. Additionally, the top priorities for the global packaging industry in 2012 are 'improving operational efficiency', 'new products and services', and 'expand in current market'. Furthermore, a total of 28% of respondents from global packaging buyers, and 36% from suppliers, anticipate a minimum of 2% increase in their current workforce. According to a research report

from GBI's, the global pharma industry is currently witnessing rapid expansion with advances in manufacturing processes, technology innovation and integration, which are the main driving forces behind the growth of the pharma packaging industry, globally. The growth is likely to be high in emerging economies like India and China, primarily on account of increasing generics and contract manufacturing activities in these countries. The fastest growth in pharma packaging market is expected from prefillable syringes and parenteral vials, which will continue to expand as advances in biotechnology result in the introduction of new therapies that must be injected. The increasing demand for biologics will boost the demand for innovative product packaging solutions in the global pharma packaging market. Also, with more than \$120 billion worth of drugs going off-patent in the next five years, generic drug manufacturers will emerge as a major segment driving demand for pharma packaging.<sup>8</sup>

Nanotechnology, the science of very small materials, is poised to have a big impact in pharma packaging and will enable it to bring innovative and new generation packaging solutions to market. Increasing demand for drug delivery devices and blister packaging will also boost the growth of pharma packaging industry. The global market for nano-enabled packaging for blisters was \$941 million in 2008 and is expected to grow to \$2.10 billion by 2014.

To conclude, India pharma packaging industry has come a long way and is due for more growth. With globalisation many MNC's in the field are setting up their manufacturing bases in India and this will further revolutionise the pharma packaging market in India. Increasing availability of better quality technology and new packaging machines in the country are some of the reasons for this rapid growth. Also the tremendous rise in health awareness amongst people will continue to create more demand for hygienic, tamper resistant and use-and-throw packaging in the future.<sup>9</sup>

Global packaging industry is worth US\$ 424 billion and out of this Europe has

US\$127 billion, Asia has US\$114 billion, North America has US\$ 118 billion, Latin America has US\$ 30 billion, and other countries have \$US 30 billion. In terms of global market percentage, Europe is 30%, North America is 28%, Latin America is 7%, Asia is 27% and other is 8% of global packaging industry. According to the materials used in packaging industry throughout the globe, paper shares the most, 36%, metal is 17%, plastic takes 34%, glass takes 10% and other occupies 3%. According to the type of packaged products, Beverages take 18%, food take 38%, pharmaceutical products take 5%, cosmetic products take 3% and other products take 36% of overall packaging industry. Global market value on food packaging is 161 US\$ billion, beverage packaging is 76 US\$ billion, Pharmaceutical packaging is 21 US\$ billion, cosmetic packaging is 13.3 US\$ billion and other is 153 US\$ billion.

#### Global market trends

Report also reveals the trend of global packaging industry, which is as below:

2004: Total market value was 405 \$US billion (approx.),

2005: The total market value was 425 \$US billion (approx.)

2006: Total market value was 440 \$US billion (approx.)

2007: Total market value expected to reach 465 \$US billion (approx.) and in the year 2008, it may reach 480 \$US billion (approx.) and by the end of the year 2014 it may touch 585 \$US billion (approx.). Presently the average annual growth rate is nearly 3.5%, which is expected to touch US\$597Bn by 2014

Pharmaceutical Packaging Industry - 2011 Yearbook provides insights into the global pharma packaging market, with coverage of the market landscape, key market trends, market drivers and restraints. The report provides market forecasts for the global pharma packaging industry until 2017.

The geographical distribution of pharma packaging manufacturers across key geographies, such as the US, the top five countries in the European region, Japan and BRIC (Brazil, Russia, India and

China) countries have been provided. Key cost and developmental issues have also been addressed. The report also provides an indepth analysis of the competitive landscape, including the benchmarking of top companies, key trends on mergers and acquisitions, and licensing agreements involving pharma packaging.<sup>10</sup>(fig1)

The global pharma packaging market was valued at \$47.8 billion in 2010. The market is forecast to grow at a compound annual growth rate (CAGR) of 7.3 per cent from 2010–2017, to reach a value of \$78 billion by 2017. The global pharma industry is currently registering rapid expansion, with advances in manufacturing processes, and technology innovation and integration, which are the main factors behind the growth of the pharma packaging industry globally. This growth is expected to be highest in the emerging economies of India and China, primarily on account of increasing generics and contract manufacturing activities in these countries.(fig2)

The pharma packaging industry will continue to grow as drugs worth \$142 billion go offpatent in the next five years, expanding the generic market and the entire pharma packaging industry. The fastest growth in the pharma packaging market is expected to come from prefillable syringes and parenteral vials, which will continue to expand as advances in biotechnology lead to the introduction of new therapies that must be injected. The increasing demand for biologics will strengthen demand for innovative product packaging solutions in the global pharma packaging market. All these factors, along with the growing pharma industry, will continue to drive demand for packaging. However, the packaging industry will have to overcome challenges, such as the availability and price volatility of raw materials and changing health regulations, in order to meet increasing demand from the growing pharma industry.<sup>11</sup>

#### CONCLUSION

The study is intended to benefit existing manufacturers of pharmaceuticals who seek to expand market opportunities. It



also can serve as a reference for pharma packaging industry players who would like to expand to nano-enabled technologies for drug packaging. This study also provides the most complete accounting of nano-enabled packaging of pharmaceutical products in various

markets around the globe. The main objective of this review is to understand the current state of nano-enabled packaging in the pharmaceutical industry, market opportunities, the companies involved, technologies being pursued and intellectual property (IP) trends.<sup>12</sup>

### Global Pharmaceutical Packaging Industry to Record Growth with Rapid Expansion in the Global Pharmaceutical Industry

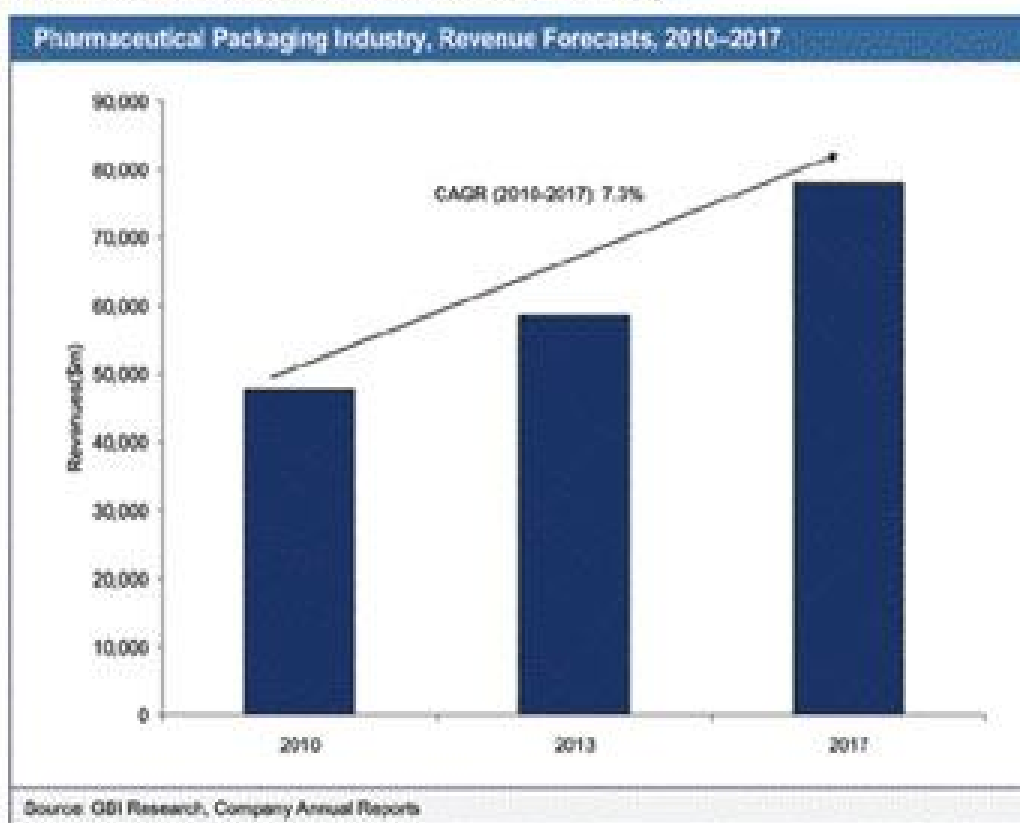


Fig. 1

Table: 1

Types of primary and secondary packaging material		
Material	Type	Example of use
Glass	Primary	Metric medical bottle, ampoule, vial
Plastic	Primary	Ampoule, vial, infusion fluid container, dropper bottle
	Secondary	Wrapper to contain primary pack
Cardboard	Secondary	Box to contain primary pack
Paper	Secondary	Labels, patient information leaflet

## Pharmaceutical Packaging Industry Will Overcome Challenges to Record High Growth Rates in the Future

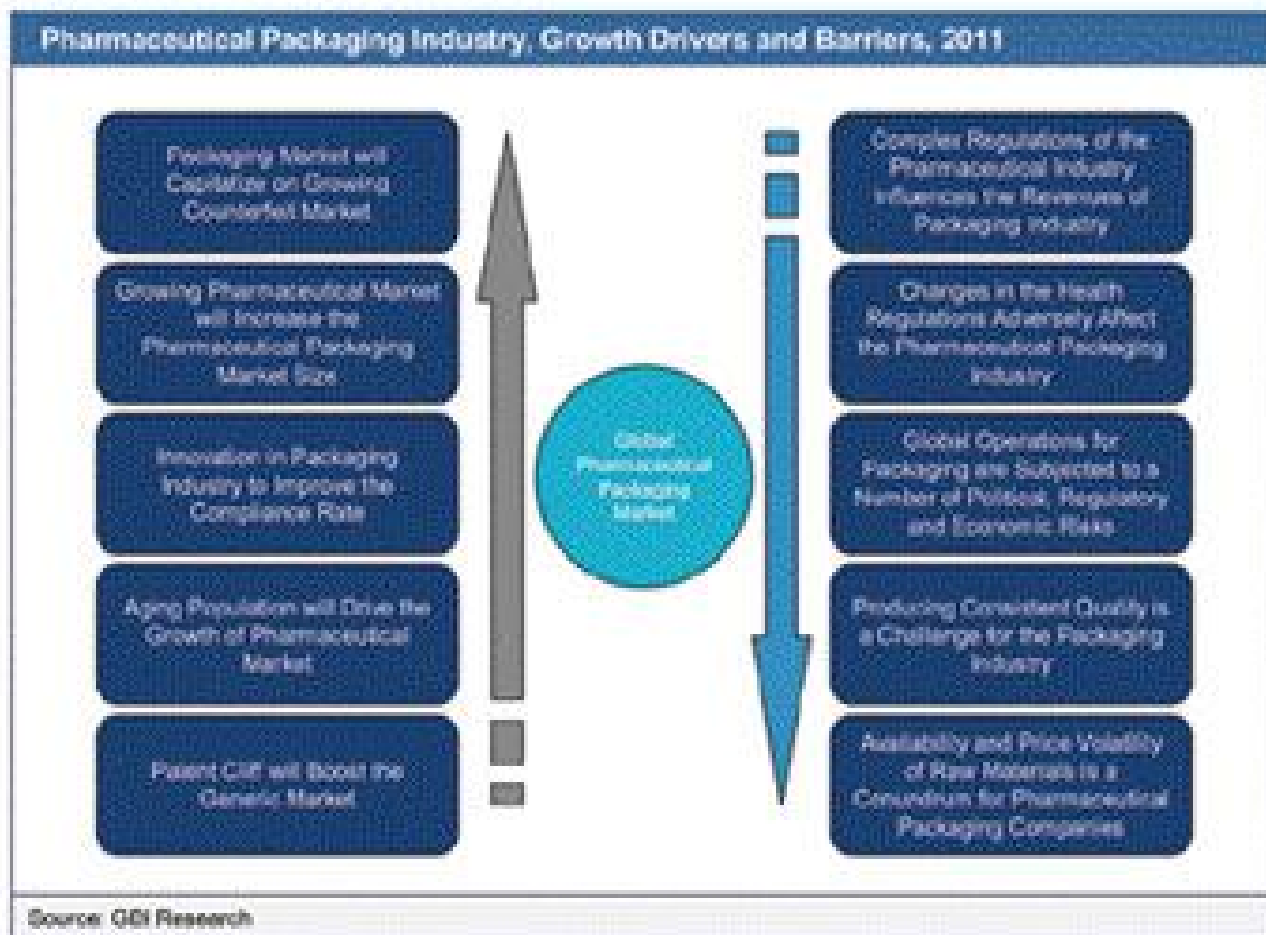


Fig. 2

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