CHANGING SCENARIO OF PACKAGING IN PHARMACEUTICAL INDUSTRY

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Abstract- Pharmaceutical packaging is one market across the globe which is advancing at a constant pace. It is expected that the market will grow day by day in the future. Packaging is a key for sale, safety and success. Like other packaged goods, pharmaceutical packaging needs to be in such a manner that it will provide speedy packaging, protection, identification, product quality, patient comfort, display and needs of security.
In the pharmaceutical packaging industry the increase of machinery for the packaging of products of drugs for rapid production.
Advancement in research of pharmaceuticals development has always been dependent on packaging technology. Maintaining integrity of
pharmaceuticals during storage, shipment, and delivery are assured by the quality of packaging available. This article reviewing current pharmaceutical
packaging trends and predicting the packaging outcomes in future.

Keywords: Packaging,Market,Pharmaceutical Industry, Biological,Production,Drugs,Machine,Medicine .

Introduction:
Packaging is defined as a technique which allows containment of pharmaceutical products from the time of production in a unit till its use. Role of pharmaceutical packaging is to provide lifesaving drugs, surgical devices, blood and blood products, nutraceuticals, powders, poultices, liquid and dosage forms, solid and semisolid dosage forms.
Packaging of pharmaceuticals essentially provides containment, drug safety, identity, convenience of handling and delivery. Pharmaceutical packaging must balance lots of complex considerations. Leaving
behind relatively simple issues such as developing good designs and communicating with customers, pharmaceutical packagers are concerned to more pressing concerns which include fighting with
counterfeiting, encouraging patient compliance, ensuring drug integrity and balancing child-resistance and accessibility for the elderly. Issue of environment safety is also a key concern for both developed and developing countries' packaging industry.
Pharmaceutical packaging firms are some of the industry's leading innovators evident by the recent advancement in technology. The current trends are result of continuous series of challenges faced by
industry. Packaging is a science which is continuously evolving and is a major success contributor for pharmaceutical industries.
Pharmaceutical packaging (or drug packaging) is the packages and the packaging processes for pharmaceutical preparations. It involves all of the operations from production through drug distribution channels to the end consumer.
Packaging also refers to the process of design, evaluation, and production of packages. Pharmaceutical packaging can be defined as the economical means of providing presentation, protection, identification , information, convenience ,compliance , integrity and stability of the product .
Effective packaging is a crucial element for the pharmaceutical industry. It protects the drug during storage, sale, shipping, and use. The packaging of pharmaceutical products also depends on the type of drug as they may react with it.
While for other products, the objectives of packaging include protection, safety, functionality, branding, and attractiveness. For pharmaceutical products, objectives include chemical protection, portion control, containment, and security of the drug as well.

Importance of Material Packaging
Product packaging maintains drug quality. It protects the product from physical damage as well as biological degradation. Some sensitive drugs require protection from light and water as they have sensitive substances. The packaging for pharmaceuticals also needs to disseminate important information. There must be proper and clear labelling—correct information needs to be disseminated.
Product packaging must protect the medicines from contamination and all external influences that may alter the drugs' property.
Product packaging is a crucial part of any product. But in the pharmaceutical industry, it is critical given the nature of the products. Life-savings drugs and medicines require the utmost care in the form of cover. Besides, stringent packaging standards also apply to pharmaceutical products.
protect a product from damage or contamination
The product must be protected against being dropped, crushed, and the vibration it suffers during transport.

Function
Packaging performs five basic functions:

The product must also be protected against the climate, including high temperatures, humidity, light and gases in the air.
To contain or hold the product and to avoid spillage or leakage during various stages of production and till it reaches the end user and he/she consumes it effectively.
To identify the product
Packaging is the main way products are advertised and identified. To the manufacturer, the package clearly identifies the product inside and it is usually the package that the customer recognises when shopping.
Protection during transport and ease of transport
A package should be designed to make it easy to transport, move and lift. A regular shaped package (such as a cuboid) can be stacked without too much space being wasted between each package. This means that more packages can be transported in a container thereby systematising logistics and supply chain.
Stacking and storage.

Types of Packaging:
There are three types of packing in the pharma industry - primary, secondary, and tertiary.

Primary Packaging
Also known as sales packaging, primary packaging is significant for pharma companies. This packaging is in direct contact with drugs and medicines. Therefore, the packaging needs to be inert and should not cause any alteration to the salt in the dosage. If the primary packaging is not done correctly, it may affect the drug, and you won't be sure about the medicine quality and its purity.
The material used for primary packaging must be neutral to ensure it doesn't interact with the pharmaceutical product during its entire life. However, if the packaging fails, the drug may become life-threatening for the patients who may consume it.
The most common material used for primary packaging includes non-reactive substances, like aluminium and PVC. Likewise, high-quality plastic is used for liquid doses instead of glass. This ensures that the products don't spill or get damaged during transportation from the factory to the pharmacy. The most common plastics used for tablets and pills include polyethylene, polyvinyl chloride, nylon, polycarbonate, and polyethylene terephthalate.

Secondary Packaging
Once the primary packaging is done, it is the time for the packaging that is called secondary packaging. It is just another layer of packaging which can be any printed material, like boxes.
All the important information is printed on these boxes, like ingredients, manufacturer's name, address, warning, and type of medicine. The printed information helps the manufacturer to distinguish between different boxes with different drugs easily. The secondary packaging essentially gives the drugs a brand image at the same time, further protects them during transportation.

Tertiary Packaging
The last type of packaging, i.e., tertiary packaging, is important for the shipping process. The end consumers don't see this packaging. The retailers often remove them before they showcase the medicines in their shops or clinics.
The main objective of tertiary packaging is safeguarding primary and secondary packaging from the external environment during storage and transportation. The most popular pharma product tertiary packaging are plane boxes, cardboards, and shrink wraps.

Types of Materials used for Packaging:
The four main categories of packing materials are as follows:
1. Glass
2.Plastic
3.Metal
4.Rubber and Fibrous Material

1.)Glass containers: These must be stiff, robust, impermeable, and chemically inert to receive FDA approval.
The pharmaceutical business uses four different types of glass, including :

1.Type I-Borosilicate glass, which is extremely durable and chemically inert. Glass's alkali and earth cations are swapped out for boron, aluminium, and/or zinc. These are used to store potent alkalis and acids.
2. Type 2-Treated soda-lime glass: Compared to Type I glass, this type is more chemically inert. "Sulphur treatment" de-alkalizes the glass surface to stop blooming/weathering on bottles.
3. Type III- Regular soda-lime glass: Soda-lime glass that has not been treated and has ordinary chemical resistance.
4. Type IV- General Purpose Soda Lime Glass: Glass is only used for products that are meant to be applied topically or orally; it is not utilised for parenterals.
Ultraviolet rays are blocked by coloured glass, which effectively shields contents from light. For this, amber glass and red glass are both employed.
The fragility and weight of glass are two of its main drawbacks as a packaging material.
2.)Plastic Containers: High-quality plastic containers of various patterns can be made with ease. These packages have a high level of leak and break resistance.

The following polymers are used to manufacture most plastic containers:

1. Polyethylene (PE): Offers a decent barrier against moisture but a somewhat poor one against oxygen and other gases. With a density of 0.91 to 0.96, high density polyethylene is used to create containers, which have four essential characteristics: stiffness, moisture vapour transmission, stress cracking, and transparency or translucency.
2. Polypropylene (PP): Polypropylene has properties similar to those of polyethylene, but it also doesn't stress-crack under any circumstances. The packaging is softened using hot aromatic or halogenated solvents. Its melting point is high.Making it appropriate for boilable containers and products that require sterilisation. One of its main drawbacks is that it is brittle at low temperatures.
3. Polyvinyl Chloride (PVC): This material can be made with an optically clear finish and offers a good gaseous barrier as well as rigidity. Reducing the amount of leftover vinyl chloride monomers further improved the quality of PVC.Glass bottles are coated with PVC to provide a shatter-resistant surface.
4. Polystyrene is a rigid, transparent material. For liquid items, useless. High water and gaseous permeability, as well as ease of stretching and breaking, are all characteristics of polystyrene. To improve their permeability and strength, polystyrene is mixed with Acrylic and rubber compounds. These are divided into three categories based on composition: moderate impact, high impact, and super impact packages
5. Nylon (polyamide) is produced by combining a large number of dibasic acids and amines. Because of its strength and difficulty to mechanically break, nylon is a very durable material. NylonOffers protection against a variety of acids and alkalis the sole drawback is that some water vapour can get through it, however this can be overcome by coating the container with PE. Not suitable for long-term product storage
6. Polycarbonate: Has the capacity to undergo repeated sterilisation. It is extremely stiff and might take the place of glass, vials, and syringes. Powerful dimensional stability and high impact are some of its characteristics.Strength, stiffness, low water absorption, transparency, and heat and flame resistance. The impact strength of polycarbonates is five times greater than that of any other typical packaging plastic.
7. Acrylic Multipolymer :These are acrylic multipolymers, often known as acrylonitrile or methacrylonitrile polymers. These allow for the packaging of goods that aren't often packaged because of its strong construction, high gas barrier, and chemical resistance.
8. Polyethylene terephthalate (PET):Condensation polymer formed by reaction of terephthalic acid or dimethyl terephthalic acid with ethylene glycol. It has excellent strength and provides a barrier for gas and aroma making it a useful package for cosmetics,mouth washes and other products.

3.)Metals: Of all the packaging materials for pharmaceuticals, metal is the most adaptable. These have exceptional physical protection, formability, durability, decorative potential, consumer potential, and recyclability. They also have outstanding barrier qualities. Pharmaceutical drugs for non-parenteral administration are packaged in metal containers, such as tubes, cans, aerosol and gas cylinders, blister packs, and packs made of foil. A few examples of the many metals utilised in pharmaceutical packaging materials are steel, tin plate, aluminium, and so forth.

Aluminium: This metal is mostly used to create laminates, foils, and seamless containers. It can be recycled to create new products and hence serves as a sustainable pharmaceutical packaging material. Recovering metal from packaging trash offers a high intrinsic value while being less expensive. Additionally, the recycling procedure does not damage the metal, allowing for the preparation of new aluminium packs using just recycled materials.Aluminum foils utilised for a number of pharmaceutical applications, such as alu-alu blister packs and inner seals for pharmaceutical containers that provide tamper evident and a hermetic barrier, can be made from pure aluminium metal by rolling it into thin sheets and then annealing them. Aluminium foil is bound to plastic film or paper to create packaging laminates with improved barrier qualities.Metalized film, which are plastics with a thin coating of aluminium metal, is an additional option to laminate packaging. Although the constituent parts of laminates and metallized films can be recycled, the difficulty of separating them hinders their economically viable recycling. These films' principal benefit is that they offer dosage forms better barrier defence against moisture, air, oils, and smells. Additionally, they feature a highly shiny surface that makes them more appealing to patients.

Tinplate:Tinplate is made from low carbon steel that has been lightly tin coated on both sides. In order to create aerosol containers and packaging closures, it is frequently employed. It is more affordable than aluminium and can be recycled numerous times into new packaging materials without losing any quality. It offers superior barrier protection, is suitable for printing, graphics, and retorting, is strong, formable, gives the dosage form a longer shelf life, and is above all environmentally friendly.

Steel:Historically, up to 40% of steel scrap was recycled to create new steel. Steels come in a variety of varieties, including carbon steels, alloy steels, tool steels, and stainless steels. It may easily and inexpensively be isolated from mixed garbage from an environmental perspective utilising a magnet. Pharmaceutical items like aerosols are packaged in primary and secondary fashion using steel containers. It is a tamper-proof packaging material that is also utilised in bottle caps and closures. Recycling steel is more cost-effective than aluminium

4.)Rubber And Fibrous Material:Latex, which is present in the sap of various plants, is used to make rubber. It serves as a closure in pharmaceutical packaging. Up to 80% of eco-friendly rubber is recycled rubber, and it doesn't contain any other harmful materials.

Fibre board :It comes in two varieties: corrugated and solid.White board is used for both the inner and outer layers of the solid board. Barrier protection is enhanced when laminated with aluminium or plastic to pack things in dry condition. Corrugated type, on the other hand, consists of two layers of kraft paper with a corrugating (or fluting) material in the centre. It is ideal for shipping product packaging because of its strong resilience to impact and abrasion.Paper has traditionally been used for pharmaceutical packaging since it is the most naturally recyclable material. Because they are entirely biodegradable and employ renewable resources for their raw components, they have a positive environmental reputation. To increase their strength and stiffness while wet, paper and board are frequently laminated with impermeable materials and coated with such materials. Although this technically makes recycling them expensive and complex, it is still possible to re-pulp these materials for use in related applications. In the production of corrugated boxes, paperboard materials are frequently employed as secondary pharmaceutical packaging.

Changes in packaging processes

In the past 25 years there have many progressive changes in packaging processes, and several significant improvements are detailed below.

Form fill seal processes for liquids and semi-liquids

The Bottlepack system (Rommelag, Germany) and a similar process by Automatic Liquid Packaging (USA)—blow fill seal—continue to be successfully used for pharmaceutical products. These processes are now found throughout the world and container manufacturing details are covered in previous chapters.

In use they usually operate in a clean area but also with a laminar flow type hood over the moulding-filling stations. With these precautions the unit can produce sterile non-preserved products. Output largely depends on the pack size, but with a 10×2 ml stick the Rommelag 3012, 305 and 4010 M machines have outputs of approx. 4,000, 8,000 and 20,000 singles per hour. The machines also offer the advantages of very low paniculate levels. ALP has a 301 and a 303–624 with six parisons coming from a single extruder giving 24 moulds. Special machines can also insert sterile components, e.g. rubber stoppers.Machines can handle PE, PP, PVC, PET, etc.

Container cleanliness

Many years ago it was common practice to store glass containers in crates out in the open. Washing was an essential prerequisite prior to use, but today producing containers and components clean in terms of both bioburden and particulates and then keeping them clean by effective handling is rapidly becoming the norm. This is now common practice in both the glass and plastic industries and, with a few exceptions (sterile and aseptic packaging operations), washing is now rarely used. (Note that rubber stoppers are normally washed (and `siliconised) at the supply source.)

Faster strip and blister packaging

Filling via slat counters into bulk packs brought speed capabilities in excess of 20,000 items (tablets and capsules) per minute, thus making small OPD type products both comparatively slow and relatively costly.

Unit dose packaging in the early years suffered from speed limitations where a maximum of 250 items per row per minute represented the best that could be achieved, i.e. the faster 4 and 8 row strip packers achieved 1,000 and 2,000 per minute (maximum) and blister packs of 8 and 12 rows, 2,000 and 3,000 per minute (maximum). Today wider webs (more rows) and higher feed speeds per row have brought about outputs of up to 7,200 in strip packs (Siebler) and over 6,000 on blister pack machines.

In addition to catering for conventional thermoformed blisters using a plastic tray and a foil-based lid, most blister machine manufacturers now offer facilities to increase moisture protection, by use of either a tropicalised blister (by an additional foil over cover) or a cold formed, foil-based tray. Considerable competition is expected between these and similar options, where a high level of climatic protection is required. The other options include blisters in sachets and overwraps to cartons. Output, climatic protections achieved, overall cost and patient/marketing preference, will influence the final pack choice.

Machine efficiency has also been improved by faster change-over times (15–30 min) and trim waste has been significantly reduced.To Improve child-resistance (see BS 7236), opaque or dark tinted packs and between-pocket perforations can be employed.

Bar coding

Bar coding, coupled to scanning and the use of computerised data/record keeping, can serve several purposes from security aspects, stock keeping and accountancy to data retrieval (i.e. product information etc). With products which are sold via various outlets (community pharmacies etc.), the EAN or ANA code is an obvious choice. This is, however, frequently used in

addition to the PIP code which was introduced by the National Pharmaceutical Association (NPA) some 20 years ago. The EAN code suffers certain weaknesses if it is to form part of a security code, and this problem may be resolved by better reading equipment or the introduction of a more user friendly code system. Coding therefore remains a highly debatable topic, with little chance of standardisation immediately in sight.

Computer Dispensing And Costing

The OPD guidelines have requested the use of the EAN code for stock control (hospitals and retail) and as a simplification for the UK Pricing Bureau where a peelable code is transferred to the prescription (form FP 10) for pricing and reimbursement to the dispensing pharmacist. The fact that other European countries have used a similar system (e.g., the Vignette, France) which was introduced many years ago does not necessarily mean that it is ideal for tomorrow's technology. Rapidly expanding computer technology could therefore bridge the gap and benefit the doctor and community pharmacist, by use of electronic transfer systems.

Original pack dispensing (OPD) (now termed 'patient packs').In any attempt to discuss future trends there must be at least a few comments on this subject. Guidelines have been agreed between the Pharmaceutical Society and the ABPI, but the most contentious issue still derives from the 7 versus 10 common denominator for solid dosage forms. Arguments have been put forward for the preference of multiples of 7 (7 day week), 4 week)(28 day/month etc.) whereas other parts of Europe are based on 10s. Since multiples of 10 appear more prevalent in Europe,

Why do we have such an insistence that UK OPD can only relate to a unit of 7? Having a pack size suitable to take a label measuring 70×35 mm also causes problems, particularly as tablet/capsule sizes get smaller and fewer doses are needed per day with delayed and sustained release products. Of course there are ways of achieving an area of 70× 35 mm, i.e. use blisters or strips in cartons or prohibit the use of container sizes below, say, a 40 or 50 ml capacity. Australia achieved this through a minimum pack size of 35 ml. This could, on some occasions, find seven tablets of small dimensions occupying only, say, 5–

10% of the container volume. This raises questions as to whether it be filled with cotton wool, and whether the high space to volume changes product stability aspects, etc.

Although there are other, less contentious issues, the proposed changes inevitably introduce on-costs to the pharmaceutical industry, the wholesaler (initial costs have been given) and possibly the community pharmacist.

Packs And Devices

In introducing product trends which could influence the pack, drug targeting was identified as an important factor. In this targeting activity, packs can be identified with an administration role or packs may be tailored to more readily fit an actual device. Examples of this include metered dose pump systems, which to some extent are replacing the well-established nasal squeeze pack.

Powder inhalation devices are currently proving very popular, in spite of the fact that patients generally prefer metered dose aerosols. However, this preference is counterbalanced by the fact that compliance is much more difficult to achieve with

aerosols. There is also a third category where the pack and the device are totally independent, e.g. a unit dose of nebulizer solution which is subsequently transferred to a pressurised or an ultrasonic nebuliser unit for delivery to the patient.

Tamper-evidence

The 1982 Extra Strength Tylenol incidents have had worldwide repercussions. Demands for a totally tamper-proof pack are difficult to achieve, certainly economically. Even so it is reasonable for a patient or user to expect that none of the product has been removed, substituted, diluted, contaminated, etc. Tamper-evidence is therefore both advisable and justifiable for pharmaceutical products provided the recipients do not expect it to safeguard them against the ingenious adulterator out to do

mischief against 'life and limb'. However, the pharmaceutical company should not be liable provided reasonable steps have been taken to safeguard the patient under normal conditions. Freak conditions, as created by the maniac, are virtually impossible to safeguard against and prevent. The use of the word 'tamper-proof' is therefore not advised, but 'tamper-evident and 'tamper-resistant' are accepted expressions.

Child-resistance

Child-resistance as such must receive everyone's support. However, child-resistance can frustrate the elderly, infirm, poor of sight, aged, arthritic, to a point where the product is transferred to an alternative (unsuitable!) pack, or the closure is never adequately replaced. There is therefore a need to recognise these problems in a growing elderly community and to find an acceptable solution. Effective answers to this, have to date, been complex and expensive.

Labelling—self-adhesive labels

Although 10 years ago the US pharmaceutical industry predominantly used heat seal labels, the UK was rapidly moving to the more expensive self-adhesive labelling systems. Since Europe is now predominantly using self-adhesive, there appears to be an international trend even though it is a more expensive label process. It has the advantage, with the correct choice of materials, that it will adhere to most substrates.

Lower microbial limits and lower particulates

The need for higher standards of cleanliness and hygiene has already been mentioned. Since the safety factors for aseptic processes and terminal sterilisation processes rely on a low initial bioburden, attempts will continue to minimise contamination. Packaging manufacturers of materials, components and containers will therefore slowly adopt GMP
procedures currently found as part of the 'Orange Guide' in order to lower both bioburden and particulates. Cleanliness and improved hygiene are an order of the day, in terms of facilities, procedures and training.Controlled dosage systems (also called monitored dosage systems)

Controlled dosage systems are basically aimed at use by the elderly, infirm, or partly infirm, poor of sight, arthritic, as an aid to improving medication compliance. Doses or dosages of medication are enclosed in individual sealed compartments on a
card, or in multiple blister packs, usually with a medication identity code (heart tablets, water tablets, etc.) together with clearly written instructions as to when each medication should be taken (day 1, 2, 3, etc. plus times, e.g. morning, afternoon,evening). These systems, of which there are now many, are already operating in the USA, Canada, Australia, Holland, and other places. However, they somewhat cut across OPD philosophies, particularly if a country is 100% OPD, since the quantities prescribed have to be transferred from bulk to the system which is then labelled or printed with the directions, solid medication codes, patient's name, etc.

The recent successes with these systems indicate that they should increase in use, subject to costs being acceptable.

Future Of Pharmaceutical Packaging

Pharmaceutical industry, research and manufacturing technologies are continuously evolving with demands of environmental ethics, patient compliance and novel medicines that have driven significant developments in packaging and delivery systems. Increased investment in the R & D sector has led to formulation of large- molecule biopharmaceutical drugs some are still in development pipelines this has led to an increase in the need for injectable packaging and self administration systems. The earlier used old glass and elastomeric closure systems may not provide the effective barrier properties much needed for high-value, life saving therapies. Packaging R&D provided us with new materials and technologies that ensure extended drug-product shelf-life. Lyophilization has led to the formulation of liposomes and further the proliposomes, the therapies which are unstable in liquid form are lyophilized or converted to dry powder dosage forms. Lyophilized drugs need special care for storage and administration for the optimal performance by products. Lyophilization chambers with proper, non-sticky stoppers are used for dose accuracy.Advancement in research of pharmaceuticals development has always been dependent on the development in packaging technology. To maintain integrity of pharmaceuticals during storage, shipment, and delivery, quality of packaging provides assurance for all these. So, development in the field of packaging is correlated with development of NDA Pharmaceuticals in the market. Use of 3D design software to design efficient pharmaceutical packages and their assessment with software's like Finite Element Analysis (FEA) need to be promoted in Pharmaceutical Packaging. This approach of virtual to real packaging can produce product right from scratch using software to create their models and then testing them with certain parameters virtually based on the data only the prototypes are created this eliminates the need for the customer to set up costly and time-consuming production runs at their sites for testing at all stages of development.

Increase in self-administered therapies forces pharmacy research to formulate packages for self administration rather than for healthcare revolving around hospital care. In present healthcare often starts at hospitals/clinics but maintenance therapy revolves around the home. For treating chronic conditions such as arthritis, cancer, multiple sclerosis, Alzheimer's and other diseases that require frequent medication, self administration had led packaging to be evolved in such a way to provide compliance for therapy. Usually maintenance therapies are delivered by injection, demanding a need for patient-friendly administration systems. Packaging systems are required to ensure that the potency of the drug must be preserved and it should promote compliance with a dosing regimen, ensuring dosing accuracy, and be as safe, easy to use and painless as possible for patients. Manufacturers involved in packaging for the self drug administration process need to provide delivery systems that will simplify drug reconstitution before use, especially for nonprofessional caregivers.

Cost and time effective packaging technology need to be enhanced in Industry. E.g., Bags with corrugated linings are developed by Jumbo bags (Chennai, India) with weight capacity of 500kgs to 2000kgs Fig. 6 [22]. These bags are cost effective then the drums normally used, also these bags require lesser area since these can be folded when not in use. Robots/ Automated devices also lead to increase in flexibility of packaging equipment, decrease in time consumption, increased output and reduced labour cost. E.g., ESS Technology, FUNAC System.

Holographic materials:

Large and important part of the security

label market and are an ideal choice for product authentication. The holographic foil, an optically variable device, is usually made using a polyester film base. The perception of the holographic image by the human eye makes it ideal for brand promotion and security. Packages reveal the holographic image when tilted against a light source. By increasing the complexity of hologram manufacturers can make it difficult for counterfeiters to duplicate the products. Many holograms besides offering brand authentication also offer tamper evident properties. If the hologram is attempted to be removed, the top polyester layer will peel off leaving the hologram on the package.

Counterfeit prevention

With counterfeiting accounting for annual losses estimated at $75bn, packaging has always been at the heart of the industry’s strategy to protect itself. It has employed an array of security techniques to combat this issue, with varying success, including : micro text, debossing and embossing,customised varnishes, holographic materials, tamper-

evident stickers, RFID (Radio Frequency Identification) track-and-trace tagging and customised graphics and fonts.

1. Ink technology: Technique allows colour to reappear when

rubbed or scratched. E.g. "Secur" labels, Ad Tape & Label, Menomonee Falls, WI.

2. Radio-frequency identification (RFID): RFID is another technology with anti-counterfeiting potential. RFID tags can help authenticate products and support data collection for pedigree records. Equipment that encodes and prints tag-equipped labels

verifies the tag before and after encoding. If a nonviable tag is detected before encoding, the label is marked with a checkerboard pattern and ejected. Good labels are encoded and rechecked. If tags read properly, labels are printed and their barcodes are verified. If the barcode doesn't scan correctly, the unit pulls the label back in, imprints it with a checkerboard pattern, ejects it, and encodes and
prints a new label "Smartline SL4M RFID" printer, Printronix Inc., Irvine, CA Fig.1 (b). For automated applications, an encode, print, and apply unit is available. It performs all the checks of the RFID printer and applies the labels at a maximum rate of 100/min "Smartline SPA8000" label printer applicator, Printronix .In multipanel labels, at least one label converter can incorporate ultrahigh-frequency (UHF) or high-frequency (HF) RFID inlays to support product security, inventory control, and track-and-trace functions "InfoPac label," Tursso Companies, St. Paul, MN.RFID can be combined with cryptography, to enable on- or off-network authentication. When the tag is encoded with the electronic product code EPC (Serialized 96-bit that can be encoded at a rate of as many as 550/min) it also receives a digital signature using public key infrastructure (PKI) based on IEEE 1363a.Dual-function tags - RFID with temperature sensing, having cost less than traditional devices for temperature monitoring e.g. integrates a sensor, microchip, battery, and antenna on a paper-thin label e.g. 13.56 MHz “TempSens " smart label, KSW-Microtec, Dresden, Germany . This type of smart sensor label–equipped blister package is being used by the National Institutes of Health (Bethesda, MD), for a multiyear study of chronic obstructive pulmonary disease that will involve nearly half a million individual doses of medication.Radio-frequency identification (RFID) tagging helps to simplify shipping, receiving, inventory location, and control has been mandated by the department of defence, several other retailers, and various hospitals. Carry and collect the data needed to track and trace products through the supply chain, prevent counterfeiting and diversion coupled with sensors to monitor conditions during shipping and storage and provide alerts if parameters are exceeded.

NFC tags

VTT Technical Research Centre: NFC tags - VTT
Technical Research Centre NFC tags are added to any packaging so a consumer could touch the code on the packaging with their NFC-enabled mobile phone to download text, audio or web page product information, which can be played back on his handset. Provided spoken dosage instructions from pharmacy staff, to aid a visually impaired or blind
person. Currently, the number of mobile phones with NFC technology is limited but VTT believes that it is a growing market.

Eco-friendly pharma packaging:

The pressure to develop sustainable, eco-friendly products is pressurising the packaging industry and has even begun to affect pharmaceutical packaging, one of the industry's most complex sectors. The development of sustainable packaging is a difficult task for companies serving the pharmaceutical industry - environmental considerations must not lead to any compromise on a package's safety or accessibility.Ecoslide-RX sustainable compliance packaging from Keystone Folding Box Company and Legacy Pharmaceutical Packaging introduces industry
with environmentally balanced formulation of packages. The pack is made from 100% recycled material, using unbleached paperboard and a clay-coated surface designed to house blister packaging with a minimum of unsustainable film and foil. The slide package meets all the modern
expectations for child-resistance and accessibility for seniors, but doesn't require heat sealing in the manufacturing process, reducing both costs
and energy usage.

Syreen prefilled syringe design:

Instead of glass, cyclic olefin polymer (COP) is used in syringes where COP provides secondary packaging altogether. Packed syringes can be clipped into places provided this eliminates the need for packaging materials like cardboard and Styrofoam. Overall packaging leads to reduction in packaging weight and volume. Syreen prefilled syringe design had extended the environmental awareness criteria to the syringe market too.

Improvising Patient Compliance

Incidence of Alzheimer’s and other age related disorders are going to be a major cause of worry in the near future. By 2020 14.2 % of the 60 age population will be In India only. This led us to work out with packaging in such a way that it will provide patient compliance with its own ease. Walmart’s new compliance pack launch is one of its kinds to help patient compliance the portable, calendar-style
prescription packs are aimed to increase patient adherence to drug regimens. Pack provides a physical printed reminder and an opportunity for consumers to see whether a dose for a certain day
has been taken or not. Greater adherence improves patient compliance/outcomes and ultimately reduces healthcare costs across the supply chainThe market today is equipped with packaging systems that can provide tracking features and product authentication throughout the supply chain. The wider use of technologies against counterfeiting will develop in near future, such as RFID tags affixed to the seal; use of UV inks for seals may be seen. The coatings with near-total barrier properties e.g., PICVD, PET-EVOH-PET, PP-EVOH-PP coatings may capture a potential market in future. 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 pharmaceutical 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 pharmaceutical 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, Pharmaceutical Packaging Industry – 2011 Yearbook.Although prediction is made based on past and future is always dependent on efforts, one can definitely predict that as pharmaceutical research will continue to develop life saving therapies, therapies for advanced life the packages required to carry and administer those therapies will also maintain its pace by advancement in design innovations and discovery through material sciences.

Controlled dosage systems (also called monitored dosage systems)

Controlled dosage systems are basically aimed at use by the elderly, infirm, or partly infirm, poor of sight, arthritic, as an aid to improve medication compliance. Doses or dosages of medication are enclosed in individual sealed compartments on a card, or in multiple blister packs, usually with a medication identity code (heart tablets, water tablets, etc.) together with clearly written instructions as to when each medication should be taken (day 1, 2, 3, etc. plus times, e.g. morning, afternoon,evening). These systems, of which there are now many, are already operating in the USA, Canada, Australia, Holland, and other places. However, they somewhat cut across OPD philosophies, particularly if a country is 100% OPD, since the quantities prescribed have to be transferred from bulk to the system which is then labelled or printed with the directions, solid medication codes, patient's name, etc.The recent successes with these systems indicate that they should increase in use, subject to costs being acceptable.

Original pack dispensing (OPD) (now termed 'patient packs')

In any attempt to discuss future trends there must be at least a few comments on this subject. Guidelines have been agreed between the Pharmaceutical Society and the ABPI, but the most contentious issue still derives from the 7 versus 10 common denominator for solid dosage forms. Arguments have been put forward for the preference of multiples of 7 (7 day week), 4 week (28 days/month etc.) whereas other parts of Europe are based on 10s. Since multiples of 10 appear more prevalent in Europe,Why do we have such an insistence that UK OPD can only relate to a unit of 7? Having a pack size suitable to take a label measuring 70×35 mm also causes problems, particularly as tablet/capsule sizes get smaller and fewer doses are needed per day with delayed and sustained release products. Of course there are ways of achieving an area of 70× 35 mm, i.e. use blistersor strips in cartons or prohibit the use of container sizes below, say, a 40 or 50 ml capacity. Australia achieved this through a minimum pack size of 35 ml. This could, on some occasions, find seven tablets of small dimensions occupying only, say, 5–10% of the container volume. This raises questions as to whether it be filled with cotton wool, and whether the high space to volume changes product stability aspects, etc.Although there are other, less contentious issues, the proposed changes inevitably introduce on-costs to the pharmaceutical industry, the wholesaler (initial costs have been given) and possibly the community pharmacist.

Batch and expiry dating

Batch coding is not new, but expiry dating is essential for virtually all forms of pharmaceutical packs. However, when and where this is printed will be an interesting topic, with ink jet printing and possibly laser printing being some of the main contenders for an on-line production operation. Laser printing, which burns off colour/printing/decoration, should be coupled to vacuum extraction for safety reasons. The legibility/clarity of debossing and embossing codes is constantly being criticised.

In-house printing

It has already been mentioned that many pharmaceutical companies serve an international industry, thereby contributing to the balance of import/export payments. Since exports frequently demand different print layouts, and one or more languages in the text, there have always been problems associated with small print runs. In-house printing is expected to increase either as a separate printing operation away from the production line or as an on-production line process. Although several printing processes can be employed, hot die stamping and thermal printing, which gives good quality print, quick drying and reasonable freedom from rub and smudging, is currently leading the field. Letterpress, direct and offset, and flexographic printing are also employed. The advent of DAR (digital artwork and reproduction) is making a major contribution to faster origination.

The need for cartoning, leaflets and packaging inserts

The USA, which is not OPD-oriented, has during the past 10–15 years moved away from the use of cartons, and leaflets have been attached to the primary pack by banding or adhesives. Although these means of attaching leaflets are available in the UK and the rest of Europe, the greater use of blister and strip pack and reluctance to change tradition should retain the carton for at least the next 5–10 years. If the move to OPD is accelerated, then a substantial growth in the use of cartons and patient (information) leaflets can be predicted. This will mean extra business for specialised printing industries, which have the security/GMP aspects of pharmaceuticals well covered.

Sterilisation methods

Although sterilisation methods may initially appear to be well documented, there is a need to review how each may change both the physical and chemical properties of packaging materials, containers and components. This entails residues related to ethylene oxide sterilisation, and physical and chemical changes when gamma irradiation or accelerated electrons are employed, particularly when plastics are involved. It should be noted that plastics include. lacquers, enamels, certain adhesives, etc. Surface analysis is emerging as a critical evaluation for any 'treatment' process. The need to establish the purity/impurity of packaging materials will also become necessary for most sterile products.

Security coding

There are many ways in which packed products can be security coded: edge slits, coloured edges, printed edges, punched hole codes, bar codes, colour bar codes, ink/ jet codes, laser codes, just to mention a few. Most manufacturers operate to some coding system which frequently adds to the total 'wording' complexities. Although bar codes plus scanning or imaging appears the simplest long-term answer, on-costs will play a significant part in any ultimate decision or solution.

Line segregation, dedicated machines and areas, cubiclisation, cleaner areas and clean air classifications

The need for cleanliness and the trend towards producing materials clean was identified above. The onus is then on the pharmaceutical manufacturer to maintain this cleanliness throughout the packaging process. There is also a need for improvements in product security with ideally a nil risk of admixtures, incorrect labelling, etc. All these aims can be optimised by clear segregation of operations, dedicated areas, the use of cubicles, operating under positive air pressure using filtered air, with properly clothed and trained operators, etc. These factors, which are all embraced by GMP, need to be supplemented by validation procedures and total accountability, reconciliation of materials delivered to and taken away from the production area. These latter security activities may be further improved by prior label scanning/reading with a possible repeat operation on a production line using such processes as 'imaging'. However, sophisticated equipment of this nature not only is expensive but requires more frequent validation. End of line inspections are therefore receiving increased attention, as are 'isolation' units for sterile/aseptic packs.

Faster lines, pregauging on-line or pregauged components and tighter specifications

Years ago the pharmaceutical industry was handicapped on output speeds, cost and security by the short runs, maximum line flexibility syndrome. This has gradually changed, particularly where companies have become international or streamlining of inventories has provided larger quantities for a few companies. Small runs, however, still frequently apply to generics.As a result of this and generally expanding sales, many companies now have dedicated lines which have moved away from 60 packs per minute to 200 to 300 packs, with better flexibility (e.g. on-line changes). High speeds have inevitably required better material control, and tighter specifications. New techniques have been introduced to negate faulty containers,components and materials either interrupting production line flow or resulting in a substandard or faulty pack emerging from the production line. These new techniques frequently involve video technology with such processes as imaging, where individual components can be matched against a standard in dimensions and the identification of imperfections. SPC is now widely applied to achieve quality improvements.

Form fill seal processes for liquids and semi-liquids

The Bottlepack system (Rommelag, Germany) and a similar process by Automatic Liquid Packaging (USA)—blow fill seal—continue to be successfully used for pharmaceutical products. These processes are now found throughout the world and container manufacturing details are covered in previous chapters.In use they usually operate in a clean area but also with a laminar flow type hood over the moulding-filling stations. With these precautions the unit can produce sterile non-preserved products. Output largely depends on the pack size, but with a 10×2 ml stick the Rommelag 3012, 305 and 4010 M machines have outputs of approx. 4,000, 8,000 and 20,000 singles per hour. The machines also offer the advantages of very low paniculate levels. ALP has a 301 and a 303–624 with six parisons coming from a single extruder giving 24 moulds. Special machines can also insert sterile components, e.g. rubber stoppers. Machines can handle PE, PP, PVC, PET, etc.

Films, foils and laminates, including co extrusions and metallisation

Although OPD is not synonymous with the use of blisters and strip packs, and products will be found in small glass and plastic containers, the unit type of pack offers possible advantages, especially when the item and quantity occupies a relatively small volume. Films and combinations of films, foils and paper as laminations,together with metallised substrates,coatings and co extrudates, etc., will all be part of an overall growth. This growth will not be related solely to thermoformed and cold formed blisters, but also to strips, sachets, overwraps, etc. and growth of shrink and stretch materials in the form of secondary packaging for warehousing and transportation. Again this may conflict with some environmental factors where composite or compound materials are difficult to recycle or reuse.

Metallisation (coatings of aluminium/oxide), which is more effective as a barrier when two materials are metallised and then laminated with the two metallised surfaces in contact, is likely to provide a better barrier than most plastic combinations(even Aclar—PVC). However, for an excellent barrier, foil of 0.025 mm and above will continue to be a popular choice as,provided the heat sealing is effective, a hermetic pack can be achieved. Lower gauges of foil down to 0.006 mm when part of a lamination incorporating a plastic ply or plastic plies also provide a high degree of protection against moisture, oxygen, carbon dioxide, etc. Although such a construction inevitably contains small pinholes, permeation through these is extremely low provided the foil layer is not stretched and/or perforated during machine handling and sealing. Coextrusion, e.g. a process incorporating two or more plies of a plastic, will undoubtedly find more use in flexible pharmaceutical packs. Coextruded can also be moulded into rigid containers, bottles, tubes, tubs, etc. subject to the quantities justifying the costs.

It is with some regret that in discussing plastics, one has to again admit that the glass—metal era is now in decline. In fact it can be positively stated that in the introduction of any new product, plastic now receives first consideration. Glass is frequently still used as a control in any test procedure, perhaps as a mark of respect for a material which has served the pharmaceutical industry with honour. The history of plastics dates back to the mid nineteenth century when celluloid and Bakelite were discovered. Bakelite (phenol formaldehyde) and urea formaldehyde, both thermosetting plastics, found wide use in the pharmaceutical industry in the form of screw closures and are still used today. Although recognised as plastics, the thermosets

play only a minor role as a packaging material and it was not until around 1953 onwards, when the first thermoplastics were used as low density polythene squeeze packs, that the real plastic revolution began. In 1996 five, in fact the most economical five, were the ones most widely used. These include the:

• polyethylenes (PE)—LDPE, MDPE, HOPE, LLDPE, ULDPE, VLDPE
• polypropylenes (PP)—homopolymers and copolymers of polypropylene
• polystyrenes (PS)—crystal and to some extent impact modified polystyrene

Conclusion

The potential applications for eco-friendly pharmaceutical packaging materials are apparently endless. The topic that can be investigated is the positive contribution that packaging makes to preserving pharmaceutical items and, by extension, the environment, despite the fact that its environmental impact is increasingly coming under investigation. Before changing any of the new environmentally friendly packaging materials, they should establish a uniform basis for use.

Standards for safe and efficient packing materials and technologies have already been established by organisations like ISO and WHO. Therefore, when using such environmentally friendly materials for packaging, the pharmaceutical industry must be sufficiently specified. As demonstrated by history, the pharmaceutical business has long used these chemicals, which can be used safely and successfully. As shown in the review, biodegradation and biocompatibility have previously been taken into account in the uses of a number of these chemicals.

The need of the day is to generate a new movement toward the production of environmentally friendly packaging materials that add value to pharmaceutical products and offer a fresh perspective on the idea of such packaging. Pharmaceutical businesses should continue to concentrate on creating a single eco-friendly packaging material that combines the best qualities of glass, metal, plastic, paper, and rubber.

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