Pharmaceutical/Medical Devices Market Assessment 2012

Market Assessment study that explores the trends and issues in the Pharmaceutical/Medical Device Industry
PHARMACEUTICAL/MEDICAL DEVICES

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# Pharmaceutical / Medical Device

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“Counterfeiting has become one of the biggest problems facing the pharmaceutical industry.”

Sr. Packaging Development Engineer
I. Executive Summary

In 2008 PMMI released a comprehensive report about the pharmaceutical industry. The current 2012 PMMI Pharmaceutical and Medical Device Industry Segment Report compares the changes that have taken place the past 5 years in the following areas:

- Patents expiring
- Innovative drug delivery methods
- Counterfeit drugs
- Offshoring and globalized manufacturing
- Worldwide spendable incomes increasing
- FDAs global influence
- Automated, integrated, smart machinery

Fifty industry professionals discussed the trends, challenges and progress in the pharma and medical device industries over the last 5 years and their conversations are the foundation for this report.

Participates included:
- 8 out of the top 10 ranked pharmaceutical companies
- 5 out of the top 10 ranked generic companies
- 8 out of the top 10 ranked medical device companies.

Overview

Much has changed the past 5 years for pharmaceutical manufacturers when it comes to packaging. Counterfeiting has become one of the biggest problems facing the pharmaceutical industry as criminals are now counterfeiting all types of products and medical devices, not just tablets or capsules. The increased threat from counterfeiting – which extends all the way to product packaging in order to fool unsuspecting consumers - has not only increased the health risk these products pose to the public, it has led to calls for the Food and Drug Administration (FDA) to impose national standards in the United States for serialization and tracking procedures. Subsequently, the clamor for FDA standards has left many manufacturers in a quandary over whether to pattern their serialization strategies after California’s impending e-Pedigree law or wait and see what the FDA does before acting.

Patents Expiring

In addition to battling the growing problem of counterfeiting, the pharmaceutical industry is facing a rash of expiring patents for brand-name prescription drugs that will result in an increase in generic drug production. More than 80 major branded drug patents will have expired between 2007 and 2016 in the U.S. In addition, drug patents will also be expiring in Japan, the United Kingdom (U.K.), France and Germany. As reported by the IMS Institute for Healthcare Informatics, once the patents on these brand
name prescription products expire in mature markets such as the United States, U.K. and European Union, spending on them is expected to be reduced by as much as $127 billion by 2016.

From a marketing standpoint, the advantage generics have over branded prescription drugs is that they use the same active ingredients as brand-name drugs and meet the same FDA requirements as their brand name counterparts, but are much less expensive to purchase. That makes them a popular choice for patients, especially in emerging markets. Consequently, each expiring patent increases the pressure on pharma manufacturers to release new products capable of replacing the expected loss in market share to generics.

**How Are Companies Reacting**

To protect their market share in the wake of competition from generics, many leading pharma manufacturers have been engineering mergers and acquisitions the past 5 years. While this trend has created a glut of used machinery in the market, many manufacturers interviewed said the excess of used machinery is only slightly delaying the purchase of new equipment. Manufacturers said that after a merger they need to evaluate the equipment’s compatibility with their existing manufacturing operations. Used equipment, despite its lower cost, does not always fit their needs.

An alternative to using mergers and acquisitions to bolster market share is diversification of product portfolios to include over-the-counter (OTC) medications. Seven of the top 10 pharma/biopharma companies are leading manufacturers of OTC drugs which are typically branded. Some leading pharma companies are even forming strategic partnerships with smaller pharma companies to produce an OTC version of branded prescription medications.

Such partnerships benefit both companies. The larger manufacturer gains access to a popular prescription drug it can market in an OTC version under its existing brand name to boost overall sales and market share, while the smaller company gains marketing and distribution resources that can enhance the brand value of its product.

Despite the trend of product portfolio diversification to help sustain and grow market share, pharma and medical device manufacturers face myriad challenges bringing new products to market, not the least of which is testing and gaining regulatory approval, which can take years.
Nevertheless, innovation remains the key to success in the pharma industry, which is why manufacturers continue to put forth drugs formulated from chemical structures never before used in clinical settings that offer patients hope of treating and eventually curing their ailment. These products are typically referred to as new molecular entities (NMEs). In addition, pharma companies are also developing duplicate therapies to compete with existing prescription and OTC medications. In some cases, these medications add a new twist, such as time release capsules or patches that can reduce the number of doses taken per day.

**Product Change Causes Change in Packaging**

With every new product comes the need for new packaging to protect it and provide easy patient access. For manufacturers, the need for new packaging typically creates a need for new packaging machinery. It’s not surprising then that pharma and medical device manufacturers surveyed cited new products as one of the primary reasons for new equipment purchases or updating existing equipment. This need has risen in importance compared to when PMMI surveyed the pharma industry in 2008. At that time the need for new equipment due to the introduction of new products ranked sixth in importance.

Changes in how medications are administered, such as unit dosage packaging that comes in blister packs, dial-a-dose syringes, inhalers and prefilled syringes, are also influencing changes in packaging. The same goes for more extensive package testing to ensure the medication is protected from elements that can degrade its quality, such as light and moisture as well as protect the product from damage during shipping.

Eco-friendly materials are another area causing change in packaging. More manufacturers are looking for ways to introduce sustainable packaging practices that enhance package quality, product safety or accessibility that don’t substantially raise packaging costs.

Medical device manufacturers, which were not surveyed by PMMI in 2008, face the same packaging challenges, all of which are happening against the backdrop of constant product innovation in both industries that is dramatically increasing the availability of healthcare around the world.

**Innovative Drug Delivery**

Innovation in packaging that can improve how patients manage their healthcare is also spurring the need for new packaging equipment. Blister packs, pre-filled syringes, transdermal patches and inhalers are all forms of packaging capable of improving patient compliance in taking a medication and make it easier to deliver the correct dosage.

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Survey participants expect use of these packaging innovations to increase.

- 1 in 5 manufacturers using blister packs expect to increase their use, while 3 out of 5 predict their use will remain the same.
- 2 out of 3 manufacturers of intravenous drugs are moving towards an increased usage of single dose injectables.
- 1 out of 4 manufacturers of inhalation therapies predict new inhalation devices in the coming years.
- 1 out of 2 manufacturers of skin absorption drug products predict growth for high-tech patches.

One of the primary packaging challenges facing pharma manufacturers is the need for stronger barriers to moisture, light, oxygen and unexpected temperature swings that can occur during shipping and compromise the integrity of the product. At the same time, better packaging is needed to prevent physical damage, such as dents or being placed under crushing weights that can break open vacuum seals, during shipping and handling.

Other challenges pharma and medical device manufacturers’ face when it comes to packaging is:

- Complying with FDA packaging regulations
- Better brand recognition
- Patient safety due to tampering
- Accurate dispensing and patient compliance
- Prevention and counterfeit detection

Having machinery that meets their primary packaging needs is only one piece of the packaging equipment puzzle for pharma and medical device manufacturers. Both are grappling with how best to produce labels containing more information about a medicine or medical device and what patients need to know when taking or using it. To accommodate the need for more labeling space, some manufacturers are using packaging inserts, extended text labels, booklet labels with peel back pages and labels featuring links to web pages that contain additional information.

Pharma manufacturers must also be cognizant of child-proofing their products without making them less accessible for seniors. While child resistant packaging protects children from accidentally poisoning themselves through the ingestion of medications containing such ingredients as aspirin, paracetamol and iron, the goal of packaging is to retain child resistant features and make it senior-friendly.

“It’s hard to incorporate the needs for an aging population in packaging when child resistant requirements need to be met, because the needs of both demographics contradict one another,” says an equipment engineer for an over the counter (OTC) pharmaceutical company. “We actually test packaging with children and seniors through our packaging research and development group.”
Key to OEMs satisfying the complex and changing needs of pharma and medical device manufacturers is an understanding of;

- How the size and scope of the pharma and medical device markets influence equipment needs
- How globalization is impacting where products are produced and packaged
- How the regulatory environment in which manufacturers must operate is changing
- What kinds of new products are fostering packaging innovation

Additionally, OEMs must understand the impact and complexity of serialization to ensure product authenticity, reduce counterfeiting and detect product diversion, as well as what expectations manufacturers have of them when it comes to developing serialization strategies and compliance.

**The Need for Serialization**

In addition to safety and patient convenience, pharma and some medical device manufacturers face a major challenge developing serialization solutions that encompass coding and data management to improve tracking and tracing their products through the supply chain. In the 2008 PMMI pharmaceutical report just one pharmaceutical company talked about complying with e-Pedigree laws. Since then, serialization has climbed to a top-of-mind discussion.

The increasing interest in serialization solutions stems from the need for pharma and medical device manufacturers to authenticate their product and provide a method for the supply chain to detect counterfeiting.

Counterfeit drugs represent an estimated 10% of all medications in the U.S., according to the FDA. In the European Union between 1% and 3% of medicines sold are considered fakes. Counterfeiting not only poses potential harm to unsuspecting patients, it undermines the reputation of a manufacturer’s brand. The World Health Organization believes that as much as 70% of the drug supply in underdeveloped countries is counterfeit.

Besides helping ensure product authenticity to healthcare providers and patients, track and trace helps manufacturers combat product diversion, whereby legitimate products are diverted from one market to another, which undermines licensing and distribution agreements. For example, a product distributor may order medications to be shipped to Europe, but the shipment is diverted to China where the product can be resold for a much higher price.

Despite the complexity and cost of aggregating product information across the supply chain, many pharma manufacturers are of the opinion their business will ultimately benefit from tracking products at the unit, case and pallet levels. However, the challenge increases as companies strive to implement a communications infrastructure that can securely store the serialized data and transfer that data through a global supply chain. Hence, the need for a global or centralized system to share serialized information is paramount.
Aggregation of product information is accurately capturing the child-parent hierarchy from the unit-to-case serial numbers as shown in the illustration to the right.

For the time being, however, the uncertainty around serialization standards and regulations remain a deterrent for the implementation of serialization strategies. California’s e-Pedigree law for tracking and tracing products across the supply chain - which is scheduled to go into effect in 2015 - will not carry the same weight as an FDA regulation. In addition, 7 other states have passed pedigree legislation and 21 others have pending serialization laws on the books in the U.S.

Although the FDA has not yet mandated serialization guidelines for track and trace, that may soon change as it has put its pharmaceutical packaging barcode rule under review due to recent high profile cases of counterfeit drugs finding their way into the U.S.

Meanwhile, pharma manufacturers producing or importing drugs into the U.S. face a dilemma over whether to develop a national serialization strategy around California’s e-Pedigree law, which will only be enforced in-state. Since there is no guarantee the California law will be the model for an FDA regulation, manufacturers do not want to create separate serialization strategies.

“Pharma manufacturers would prefer guidance from the FDA on how to do serialization and provide standards,” says a pharma industry consultant.

In the absence of a global standard, as well as an FDA standard for the U.S. manufacturers must navigate what regulations are in place on a country-by-country basis, which makes compliance a challenge. Some manufacturers are either tabling serialization development efforts or slowing development of current serialization strategies until there is a clearer picture of the regulatory landscape.

**Globalization and Offshoring**

The trend toward globalization has not only provided a boon for pharma and medical device manufacturers in the form of sales to new markets, it has opened the door to lower cost manufacturing by locating plants in countries where:

- Low-cost labor is abundant
- Regulatory guidelines are more lenient
- Highly attractive tax rates are offered
Thanks to globalization, sales of pharmaceuticals are expected to grow from $956 billion ($U.S.) in 2011 to $1.2 trillion in 2016.¹ Medical devices, on the other hand, have two different projections in the industry. The Medical Device and Diagnostic Industry magazine pegs medical devices to be a $350-billion industry globally.² Espicom projects the industry to reach $307 billion in 2012 and rise to $434 billion in 2017.³

With global demand for pharma products and medical devices rising, U.S.-based manufacturers in both industries are locating plants outside the U.S. to not only produce closer to distant global markets, but take advantage of the cost, financial and regulatory benefits of manufacturing abroad.

**Figure 1: Shifts to manufacturing offshore**

In the first grouping of bars in Figure 1 to the right:

- 38% of pharma manufacturers see an increase in offshore production with those products being imported back to the U.S., compared to 34% in 2008.
- 50% of medical device manufacturers see an increase in offshore production with those devices being imported back to the U.S.

“We are increasing our offshore manufacturing due to tax advantages and low overheads and reduced labor costs,” says a packaging engineer for a medical device manufacturer. “Our CEO’s number one goal for now is to design, source and build closer to market.”

Manufacturing as close to the market as possible ensures better time to market, better patient feedback and an improved ability to meet regional requirements, according to a senior packaging engineer for a pharma and medical device manufacturer. For these reasons, some leading pharma companies are closing existing plants in the U.S. as soon as prescription drugs come off patent and re-establishing them in countries where it is much cheaper to produce the product as a way to offset the loss of revenue due to competition from generics, according to the managing director for a compliance surety consultancy.

Assumingly, the FDA has expanded its influence on manufacturers that produce outside the U.S. and import back into the country.

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62% of the manufacturers interviewed for this report expect an increase in FDA-approved facilities overseas, compared to 20% in 2008.

The most often mentioned locations are the Asia Pacific region, particularly China and India.

In addition to more regulatory oversight, the FDA is expected to expand its reach when it comes to process validation and equipment qualification for offshore plants.

According to the director of engineering at a global pharma leader, there needs to be a more "level or fair" playing field globally so that inspections for both domestic and foreign manufacturers are conducted equally. Currently, overseas facilities are not inspected on a regular basis while domestic facilities are inspected annually, which is a problem, he added.

As more manufacturers set up plants around the world, they are looking to source their processing and packaging equipment from global suppliers, as opposed to suppliers in each market. In 2008, U.S. OEMs were the supplier of choice with 58% of companies purchasing most of their equipment from U.S. OEMs, compared to 42% purchasing from offshore manufacturers (Figure 2).

**Figure 2: Equipment purchases, U.S. versus offshore**

In 2012, that trend reversed. 59% of pharma manufacturers are purchasing more of their equipment from offshore suppliers, compared to 41% of pharma manufacturers purchasing more of their equipment from U.S. suppliers. Medical device manufacturers are following suit with 55% purchasing more of their equipment from offshore suppliers and 45% purchasing from U.S. suppliers.

Typically, secondary packaging equipment is sourced from U.S. manufacturers, like case packers, palletizers, cartoning equipment and over wrap machinery. In comparison, labeling and filling equipment and blister pack machines are typically sourced offshore. “There are a limited number of pharma processing equipment manufacturers in the U.S. so this equipment tends to come from Europe,” says an engineer from a pharmaceutical company of prescription drugs.

**The Role of Contract Manufacturers**

Just as pharma and medical device manufacturers are looking to set up plants offshore to take advantage of cost reductions, they are turning to contract manufacturers and packagers not only for cost savings, but to gain greater flexibility for packaging smaller batches and to gain a local presence.
Today,

- 42% of pharma manufacturers and 21% of medical device manufacturers using contract packagers plan to increase their reliance on contract manufacturers.
- 32% of the pharma manufacturers and 36% of medical device manufacturers using contract packagers expect their reliance on contract packagers to remain the same.

In 2008, the trend toward a greater reliance on the use of contract packagers was just emerging. At that time, 88% of manufacturers planned to increase their relationships with contract manufacturers and just 8% expected their use of contract manufacturers to remain the same.

Then, as now, the advantages of using contract manufacturers and packagers remain the same:

- Saving on capital costs
- More flexible line changes
- Reducing the number of dedicated in-house packaging lines
- Obtaining local presence
- Smaller batch runs

**Sustainability and Eco-friendliness**

Sustainability continues as a key trend among pharma and medical device manufacturers, as it has across multiple segments of the packaged goods industry, because of the proven benefits sustainability brings to the environment and the bottom line.

The rising cost of raw materials is making packaging a greater percentage of the total, which is prompting some manufacturers to seek out materials that are less expensive. Also impacting the cost of packaging is the rising cost of energy needed to operate the production line, which is driving manufacturers to consider more energy efficient equipment.

Pharma manufacturers continue to implement similar sustainable strategies today as they did 5 years ago to increase the efficiency of their packaging lines and lower their overall operating costs and medical device manufacturers are jumping on the bandwagon for the same reasons. Those reasons include:

- Reducing the overall amount of packaging material used
- Using eco-friendly materials made from recycled packaging
- Thinner gauge materials that do not compromise the strength or protective qualities
- Minimize and reuse waste materials
At the same time, pharma and medical device manufacturers are looking for packaging machinery that can not only handle the new generation of eco-friendly packaging materials without jamming, but which reduce energy, air and water consumption to lower their overall carbon footprint and run their plants more efficiently.

“We have a big focus on sustainability, reducing corrugate weight and finding the lowest level of packaging weight, and still being able to retain sterility,” says a packaging engineer for a medical device manufacturer that produces procedure trays for minor surgery.

**Future Machinery Needs**

As is the case with manufacturers in many industries the primary needs in new packaging equipment are:

- Greater flexibility in changing over product lines
- Easier cleaning
- Less maintenance and more diagnostic alerts
- Higher operating speeds for faster throughput
- Improved operator safety
- Intuitive, user-friendly HMI

The need for more flexible changeover is being driven by an increase in the number of different SKUs run on a packaging line, which can be as high as several hundred. Different types of SKUs mean more product changeovers and the longer it takes to complete a changeover the more downtime and less productivity on the line.

Validation, the process by which any change in the packaging process is treated as a product/process design change and must follow a full design change procedure, is a major and complex undertaking for manufactures. Documentation is required for compatibility and integrity, shelf life, sterile barrier and distribution testing of the packaged product.

Just as in 2008, manufacturers are looking to OEMs to help them with:

- Equipment validation and qualification
- Documentation, particularly for FAT, IQ, OQ, PQ
- Demonstrate good manufacturing practices

Another underlying factor driving new equipment purchases is the opportunity to introduce more robotics into the packaging line. What makes robotics attractive is a greater efficiency compared to manual processes such as placing primary packages into secondary packages and placing secondary packages on to pallets.

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4 FAT-Factory Acceptance Testing. IQ-Installation Qualification, OQ-Operation Qualification, PQ-Performance Qualification
Manufacturers are also looking for control systems, operating interfaces and safety systems standards to minimize human contact with their packaging machinery and improve quality control, operating efficiency and operator safety. In addition, manufacturers also expressed a need for real-time global production data. Two out of three manufacturers say they need machinery capable of capturing and communicating performance— an indication this trend is becoming more important.

Better training for machine operators remains a critical component in the purchasing decision. Knowledge of Key Performance Indicators (KPI's) among personnel on the plant floor is key to operating efficiency and troubleshooting minor issues before they become full-blown problems that require the line to be shut down.

Finally, manufacturers are looking to OEMs to help them support aging equipment by improving

- The availability of parts
- Helping raise safety standards
- Integrate smarter components
- Communications and recommend equipment improvements as needed

**Be a Manufacturing Partner**

By taking the time to understand the needs of manufacturers, OEMs can build machines that improve operations when it comes to;

- Flexible changeover
- Robotic solutions
- Validation
- Real-time data capture / analytics
- Operator safety

OEMs are being asked to be a manufacturing partner, which can be achieved through:

- Regular on-site visits to assess equipment requirements
- Suggesting specialized equipment to replace aging machinery
- Designing new machinery that answers the challenges of the future

In doing so, OEMs will not only deliver better solutions, but deepen relationships with pharma and medical device manufacturers at a time when their business are undergoing tremendous change.
Report
Findings

“There needs to be a more level playing field globally so that FDA inspections for domestic and foreign manufacturers are conducted equally.”

Director of Engineering
Manufacturers face a variety of challenges ranging from designing packages that protect medications and medical devices from harmful elements that can compromise product quality, fighting counterfeiting and encouraging patient compliance to balancing the need for child resistant features with easy access for elderly patients.

The opinions and predictions from 50 pharmaceutical and medical device professionals are summarized in this 2012 PMMI Industry Segment Report. The report is structured with five categories:

I. **Drug Delivery Trends**
Manufacturers must stay atop of packaging trends as patented drugs expire and give way to an increase in generic drug manufacturing. There is a growing trend toward single dose dispensing through blister packs and pre-filled syringes, and to a lesser degree high-tech transdermal patches and enhanced inhalers. Incorporating more information on labels that describes how to take the medication and the potential side effects is an ongoing effort for many manufacturers.

II. **Global Shifts and Projections of Growth**
Global growth is prompting many manufacturers to set up plants offshore to better service emerging markets. Subsequently, they are looking to source equipment and packaging materials in local markets whenever possible. The shift to offshore manufacturing is causing concern amongst industry professionals that offshore plants are not being held to the same FDA standards and inspection as U.S. manufacturers.

III. **Trends in Packaging**
Manufacturers are increasingly working with sustainable packaging materials that do not raise the cost of packaging while initiating efforts to reduce material waste and energy consumption on the packaging line.

IV. **Machinery of the Future**
The equipment needs of pharma and medical device manufacturers are complex. The majority of manufactures are looking for equipment that offers greater flexibility and faster changeover between product runs, is easier to clean, presents a modular design and incorporates the integration of robotics as well as captures machine performance for process validation and improves operator safety.

V. **Visions of the Future**
Manufacturers need OEMs to be partners. Consistent communications will result in machinery design that meets their needs in the next generation of equipment as well as supports aging equipment. They are looking to the OEMs to aid in machine validation and qualification, adhere to good manufacturing practices and provide documentation for IQ (installation qualification), OQ (operation qualification), PQ (performance qualification) and FAT (factory acceptance testing).
I. Drug Delivery Trends

A key element of pharma and medical device manufacturers’ growth strategies - product development - is also the number one reason for purchasing new equipment. Indeed, new patent protected drugs and medical devices ensure manufacturers the opportunity to reap substantial profits and market share in the absence of competition from lower cost generic versions. New product research and development is a costly and time consuming process. It takes an average of 12 years and hundreds of millions of dollars for a new medication to move from the laboratory through clinical testing in order to receive FDA approval and finally reach the market. Only 10% of tested medications ever receive approval, according to the California Biomedical Testing Association.

Once a new drug is FDA-approved it needs to be packaged for delivery to the patient. Increasingly packaging is playing a key role in the delivery of many new medications to enhance patient compliance. For example, tablets and capsules are often placed in calendar or wallet-type blister packs that can aid patients in remembering whether they have taken their medication simply by looking at the instructions on the package or counting the doses taken.

As shown in Figure 1 below, oral medications remain the dominant form for medications with 51% market share. In comparison, intravenous or parenteral drugs account for 29% of the market, inhalable drugs 17% and transdermal patches and creams 3%.

![Figure 1: Market share of drug delivery methods](image)

Reasons why packaging plays a key role in the delivery to patients include:
- Convenient dispensing of the medication
- Protection from contamination and degradation from the environment
- Ensure child resistance, yet be senior-friendly

Given these criteria, plastic bottles remain the most common type of packaging in the U.S. for prescription and OTC oral drugs distributed in bulk to pharmacies in tablet or capsule form. Nevertheless, use of plastic bottles for packaging oral medications has been slowing as other forms of packaging, such as blister packs, gain momentum because of their ability to deliver unit dose or unit-of-use packs for prescription and OTC tablets and capsules.
Blister Packs

Unlike medications that are packaged in a bottle, blister packs contain individually wrapped pre-measured dosages thereby helping to ensure patients are taking the correct dosage.

Other advantages of blister packs include easy dispensing and better overall product hygiene through hermetically sealed packaging. As a result, blister packs are one of the fastest growing segments of pharma packaging.

“Blister packs have seen double digit growth the past several years,” says a pharma industry consultant.

According to a vice president of packaging technologies for a pharma manufacturer, blister packs account for about 10% of packaging for pharma drugs in the U.S. In addition, more than 240 million or 7% of the 3.4 billion prescriptions filled annually in the U.S. use some form of calendar or blister packaging.

“In Europe, blister packs are used in 85% of pharma prescriptions and there is a movement towards it in the U.S. Walmart is a big user of blister packs and it is very common for birth control pills,” he says.

Although Walmart is embracing blister packs for some pharma products with their introduction of Ecoslide-RX last year, a compliance pack that is environmentally sustainable, a project engineer for at a leading pharma company says the retail giant no longer wants blister packaging for disposable syringes. The project engineer added that he foresees the use of blister packaging for medical devices decreasing slightly in the future.

Figure 2: Market share of blister packs versus bottles

Of those companies participating in this report as shown in Figure 2 to the left:

- 28% of their product mix has moved to blister packs
- 72% remains in bottles

Manufacturers also like blister packs because they can create so-called flat pack cards containing a multi-week supply of medication that is easier for insurance companies and direct-to-consumer retailers to send to consumers via the mail.

Clear blister packs can also help patients become familiar with the size, color and shape of their medication, enabling them to spot suspicious characteristics sooner, which is another line of defense against counterfeiting.

Blister packs provide a method for:

- Better patient compliance
- Improved product stability
- Longer shelf life
While those advantages have proven viable, 64% of the pharma and medical device manufacturers interviewed, however, do not expect their overall use of blister packaging to increase. One reason frequently cited is that blister packs cost more to produce, which can make them impractical for packaging large pill counts.

“Blister packs cost more to produce and it’s cheaper, faster and easier to put large pill counts in bottles,” says a senior packaging development engineer for an OTC pharma manufacturer.

“For less than 10 pills blister packs are used for better shelf space and for additional text needed on the package. Larger size pill counts will remain in bottles, which helps with theft prevention,” he continues. “For over the counter products, blister packs are used to compete with other blister packaging and to take up more shelf space which is appealing for brand awareness.”

As the popularity of blister packs grows pharma manufacturers are finding a wide variety of uses for blister packaging beyond encapsulating pills. A manufacturer of generic pharma products and some medical devices is using a thermoformed rigid tray sealed with film to create 6 or 8 unit blister packs for catheters and single dose syringes. Blister packs account for 40% of the packaging used by the company, according to a senior plastics engineer.

**Figure 3: Predictions of blister pack usage**

Of the pharma manufacturers and contract packagers interviewed:
- 18% said they expect to decrease their use of blister packs and move back to bottles
- 64% said they expect the ratio of blister packs to bottles to remain the same
- 18% said they expect to increase their ratio of blister packs to bottles

Although most manufacturers do not expect to increase their use of blister packs, demand for the packaging is projected to be stronger in emerging markets. “We will have new blister volume over the next couple of years for Latin America,” says the senior packaging development engineer for an OTC pharma manufacturer. He adds the company expects to shift its ratio from bottles to blister packs increasing from 20% to 25% in the next few years.

**Oral Drug Delivery Methods Gaining Popularity**

Looking ahead, some of the oral drug delivery methods gaining popularity or under development that pharma manufacturers expect to influence packaging at their plants include:
- Prefilled doses like cups or stix packs
- Medicinal powders put into drinks
- Slow release pills
- “Quick solves” that dissolve on the tongue
- Caplets that are easy to swallow (expected to grow over the next 10-15 years)
- Drugs with a combination of ingredients
- Chewable (such as gummies)
- Foam based products (which are in the development stage)

Due to the growing sophistication of oral medication forms, one packaging engineer for a manufacturer of generic medications and nutraceuticals predicts there is likely to be a need for additional cold chain shipping to provide better humidity and temperature control for oral drugs during shipping.

**Parenteral / Intravenous Methods**

Another form of drug delivery gaining popularity are prefilled syringes that come in the shape and size of a pen, making it easy for patients to carry them in a pocket, purse or carrying case. Already commonly used to deliver insulin, pre-filled syringes typically come with a self-contained cartridge that can be loaded into the syringe, thereby eliminating the need for patients to measure the dosage received.

Prefillable syringes are predicted to represent the fastest growing aseptic packaging type as advances in biotechnology lead to new therapies that must be injected, with demand expected to grow 11% each year to $1.1 billion by 2016.\(^5\)

While primarily thought of as disposable packaging, prefilled syringes can be reused. Some pharma manufacturers are also producing prefilled syringes that allow the patient to adjust the dosage in small increments using a dial on the device.

“I foresee more pen injectable dosage formats being used, like a dial-a-dose for diabetic meds,” says the equipment engineer for a leading OTC pharma company. Indeed, 2 out of 3 companies that manufacture intravenous drugs participating in this report predict increasing their usage of single dose injectables.

Other reasons stated for moving to pre-filled, single dose syringes include:

- Improved needle safety and sterility
- Ease of use
- Therapeutic proteins development for cancer drug injectables
- Use for a variety of procedures – cosmetic, dental, veterinary
- Packaged in multi-dose vials to reduce the cost to the customer

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\(^5\) Source: January 2012, Freedonia
**Inhalation**

Inhalants are also expected to become a more popular method for delivering medications. Driving the interest in inhalable medications is their rapid absorption into the body through the lungs and that they offer a quick, convenient method for taking medications.

Currently, inhaled medications are primarily made for the treatment of respiratory ailments. “Inhalation therapy is supposed to be the best delivery system,” says a vice president of packaging technologies at a pharmaceutical company. 1 in 4 pharma companies that manufacture inhalation therapies continue to move toward developing these products.

A project engineer for a pharma company added that some intravenous medications are being converted to inhalable drugs to avoid needle sticks. “Inhalable drug delivery devices will improve in the next two years,” adds a project engineer for a leading pharma company.

**Transdermal**

Transdermal or medicated adhesive patches continue to gain ground as a drug delivery method because they provide a controlled release of the medication into the patient that can be superior to oral, inhaled and intravenous medications.

Despite their superiority when it comes to controlled release of a medication into the body, transdermal patches, which became commercially available in the U.S. in 1979, remain a niche product with 3% market share.

As for future growth, the director of packaging component sourcing for a pharma company said that while there is movement to OTC patches and creams, momentum behind the trend is building slowly. An industry expert predicts more oral drugs will become available in transdermal patches to avoid some of the absorption problems caused by a patient’s metabolism and avoid potential irritation of a patient’s stomach. It is a trend that has seen double digit growth the past 10 years, he adds.

While only a few companies interviewed manufacture transdermal medications, half of the pharma companies that manufacture skin absorption drugs predict growth potential for hi-tech patches.

A senior packaging development engineer at a pharma company specializing in pain remedies concurs, saying: “We’ve been getting into this area for the past two years and see big moves toward expanded usage.”

Despite the optimism surrounding the growth of transdermal patches and creams, some pharma manufacturers temper their growth projections. “Hi-tech patches are increasing a bit, but it’s really more of a novelty,” says a project manager for one of the leading pharmaceutical and OTC manufacturers.
Ask Your Customer
By taking the time to understand how pharma and medical device products evolve and impact packaging, OEMs can design machinery best suited to meet the increasingly complex packaging needs such as:

- Barrier protection from elements that can degrade product quality
- Temperature protection during transportation
- Display vital information patients need to know about usage
- Innovation to enhance the manufactures brand
- Assure safe travel through the supply chain

II. Global Growth and Shifts in Manufacturing

The expanding global economy is boosting consumer incomes in emerging countries where pharmaceuticals and medical devices are becoming more available to patients. At the same time, increasing consumer demand for better access to healthcare and better outcomes from medical treatments is paving the way for medicine and medical devices to play a more important role in worldwide patient care.

Global Demand Rising in Emerging Markets

It’s not surprising then that the global demand for pharma products and medical devices is on the upswing. The global pharmaceutical industry, as show in Figure 4 to the right, is projected to emerge from its current modest growth phase of 3% to 4% CAGR (Compound Annual Growth Rate) and rise to 5% to 7% annually in 2016. Global sales will total about $1.2 trillion in 2016, up from about $956 billion in 2011, according to the IMS Institute for Healthcare Informatics in a July, 2012 report.

Leading the expected global growth wave for pharma products and medical devices will be emerging markets, the largest of which are China, India and Brazil. The demand for medical products in these countries is expected to more than offset slowing growth in mature markets such as the U.S., Canada, Europe, Japan and South Korea.

Spending in emerging markets is expected to double the next 5 years, growing to an estimated $150 billion to $165 billion, according to IMS. By 2016, emerging markets will represent 30% of global spending on medicines, compared to 20% in 2011.
Mature Markets Lose Global Market Share

In comparison, according to IMS, the outlook in mature markets (U.S., Europe, Japan) is not as robust. Mature markets’ share of global pharma spending is expected to fall to 57% in 2016 from 66% in 2011. The decline in the U.S. is expected to be particularly sharp, falling to 31% in 2016 from 41% in 2006.

Declining sales volume in mature markets will largely be driven by expiring patents on top-selling brand name prescription medications. As those patents expire, lower cost generic versions will enter the market and pull market share away from brand names. The brunt of this trend will be felt in the next year as at least nine top-selling prescription drugs such as Plavix, Seroquel and Singulair, have their patent protections expire.

By 2016, however, the impact on sales in the U.S. from expiring patents is expected to be significantly less, when just four patents for major prescription drugs are scheduled to expire. In addition, U.S. pharma sales are expected to receive a projected $6 billion sales boost in 2014 due to increased medication demand as more consumers obtain health insurance policies with prescription drug plans under the Affordable Healthcare Act.

Figure 5: Shift from branded to generic drugs

As many leading pharma manufacturers head toward the so-called patent cliff, its impact on the sales of branded prescription drugs is expected to be felt globally. The share of global spending on branded prescription drugs, as shown in Figure 5 to the left, is expected to drop to 53% in 2016 from 63% in 2011, according to IMS.

Meanwhile, share of global spending on generic prescription drugs is expected to reach 35% in 2016, up from 25% in 2011. During the next 5 years about $106 billion in consumer spending is expected to shift to generic drugs. Share of global spending on OTC drugs is expected to remain consistent during that period. All other products which include OTC will remain the same at 12% market share.

Spending on Pharma Packaging

Despite slowing pharma sales in mature markets, growth in pharma packaging is expected to be robust, growing to a $78 billion market in 2017, up from $47.8 billion in 2010, according to Freedonia Group.

In the U.S., pharma packaging is projected to grow 5.5% annually through 2014 according. Growth will primarily be driven by new packaging standards and regulations to address barrier protection, infection control, patient drug compliance, drug-dispensing errors and drug diversion and counterfeiting.
Medical Device Outlook

After weathering a multi-year slowdown that began in 2008, global sales of medical devices began to rebound in 2011. There are two different predictions in the industry and both are reported here. Annual growth rates are projected to hit 7.1% CAGR between 2012 and 2017, according to market research firm Espicom. As shown in Figure 6 below, during this period, global annual sales of medical devices are projected to total $434.4 billion, up from $307.7 billion currently according to Espicom, and up from $350 billion according to Medical Device and Diagnostic Industry, which predicts growth of 3% to 4% CAGR for the global medical device industry.

Figure 6: Global growth in medical device spending

Just as in the pharma industry, emerging markets, especially China, Russia and Brazil, are expected to propel sales growth thanks to a combination of government investment in the healthcare system and a growing need for imported medical devices to compensate for the lack of in-country medical device manufacturers.

The Chinese government has been building thousands of hospitals, healthcare centers and clinics since 2009 as part of a long range plan to provide universal healthcare to its 1.3 billion citizens by 2020. As a result, spending on medical devices to stock these facilities is projected to grow exponentially in the near-term. The U.S., Germany and Japan were the leading supplies of medical devices to China in 2011.

In Russia, annual sales of medical equipment and supplies are estimated to reach $5.4 billion in 2012. Helping propel the growth of the country’s healthcare system is a government initiative launched in late 2010 to boost local production of medical devices to 50%. Currently, about 73% of medical devices are imported from the U.S., Germany and the Netherlands, according to Espicom. Those three countries account for about 53% of medical device imports, which have been increasing in value year-over-year since 2008.

In South America, Brazil represents the largest medical device market in its region, as well as the largest economy. Even though hi-tech medical device imports account for a small portion of Brazil’s economy, about $2.6 billion in 2011, about 70% of all imports come from medical device manufacturers in the U.S. or Europe, according to Espicom.

Further boosting prospects for sales of medical devices in Brazil is continued expansion of the private health insurance sector, which is paving the way for better medical care through improved access for patients to equipment and devices. At the same time, the government is modernizing and upgrading medical facilities and equipment, a trend expected to bode well for medical device manufacturers.
The Foothold of Overseas Production

More than half of manufacturers surveyed see the demand for their products growing in the Asia-Pacific region in the next 5 years, particularly in China and India as shown in Figure 7 below. 1 in 5 companies are seeing increased demand for their products in South America.

Figure 7: Product demand growing most rapidly in emerging countries

With demand for medicines and medical devices growing globally, manufacturers are facing choices when it comes to which countries they produce their products.

Among the advantages to be gained from locating plants outside the U.S. are:

- Lower labor costs
- Tax advantages
- Overall cost reductions
- Lenient regulatory environment
- Cheaper raw materials

A packaging engineer for a leading pharma and medical device manufacturer says: “Manufacturing offshore and importing back to the U.S. is always considered for the tax benefits.”

The difference in corporate tax rates levied in countries outside the U.S. can be quite substantial. In Ireland the tax rate is 12%, in Singapore its 5%, in the U.S. its 29%, according to one pharma manufacturer.

A growing trend of offshore manufacturing is that many of the pharmaceutical products and medical devices produced outside the U.S. by U.S.-based manufacturers are imported back into the country. At least half of all medical devices used in the U.S. are imported, while about 80% of active pharmaceutical ingredients in medications sold in the U.S. are manufactured elsewhere, according to the FDA.

“We see the manufacturing of products offshore and shipped back to the U.S. increasing,” says the head of technology for a contract packager. “We purchase tablets that are manufactured in Asia/China and are imported back into the U.S. for packaging.”

In 2008, 34% of pharma manufacturers said they were increasing offshore manufacturing and U.S. imports as shown in the orange bar in Figure 8 on the following page. The two leading destinations were China and India. An equal amount said that manufacturing will remain in the U.S. and it was mainly due to FDA compliance and the threat of counterfeit drugs coming from offshore.
Figure 8: Trend in offshore manufacturing and importing back to the U.S.

Those percentages have shifted in the last 5 years. Today 50% of medical device companies and 38% of pharma companies report they are manufacturing offshore.

“Offshore manufacturing is not necessarily increasing but those manufacturing offshore are staying offshore for cheaper labor and to avoid tax implications and regulatory implications,” says the vice president of packaging technologies for a pharma packaging company.

Offshore Manufacturing Sites

India and China are two countries pharma companies typically look to when establishing new manufacturing plants, in addition to the U.S. Commonwealth of Puerto Rico. Other countries where pharma manufacturers locate plants outside the U.S. include Africa, Australia, Czechoslovakia, Ireland, New Zealand, Poland, Sweden and the United Kingdom.

One leading pharma manufacturer said it operates plants in more than 70 countries. Another manufacturer of pharma, Rx and injectable aseptic products said it has plants in 40 countries.

Countries outside the U.S. where medical device manufacturers are producing products include China, Brazil, Germany, Ireland and Japan. Puerto Rico, long considered to be a low-risk destination for offshore manufacturing of medical devices and pharma products, is another popular locale for manufacturing outside the continental U.S.

When pharma and medical device manufacturers were asked which region is likely to be the next FDA manufacturing center, China, India, Ireland and Brazil were most frequently mentioned.

Maintaining Quality Control Offshore

Despite the popularity of offshore manufacturing, some companies interviewed said they are considering returning production to the U.S. Some of the reasons cited include:

- Compliance issues
- Improved product quality
- Better control of the supply chain
- A more costly exchange rate for the Euro
Of all the reasons cited for returning manufacturing back to the U.S., quality control is arguably the most influential. A reduction in quality can not only lead to fines totaling as much as hundreds of millions for non-compliance with FDA requirements for products exported back into the U.S., it can seriously damage a manufacturer’s reputation through bad press. The latter is often considered to be more costly to a company in the long run than any fine.

The biggest challenge pharma and medical device manufacturers face when locating a plant offshore is transferring the intellectual knowledge from its U.S. headquarters to the plant. Barriers to transferring this knowledge include differences in language and cultural values.

To ensure quality control for products manufactured offshore and imported back into the U.S., most of the pharma and medical device manufacturers interviewed said they foresee an increase in the number of FDA approved plants offshore.

Figure 9: Predictions of FDA approved manufacturing sites increasing offshore

In 2008 only 20% of the manufacturers predicted that FDA-approved facilities would be located offshore. Predictions of FDA locations in China or India were far in the future.

Five years later that picture is quite different with 62% of companies stating that FDA facilities offshore continue to increase with the majority of those appearing in the Asia Pacific region.

Today’s predictions that more FDA-approved plants will be located offshore is a major shift from 2008 when 51% of manufacturers predicted the U.S. would remain the strong hold for FDA-approved manufacturing facilities due to the difficulty and cost for FDA to audit offshore. Those predictions were partly true.

While the U.S. remains the epicenter for FDA-approved facilities, one reason cited for the increase in FDA-approved plants offshore is to ensure equal inspections for foreign and domestic plants to level the playing field. The intent does not meet the action as offshore inspections are not occurring with the same frequency global manufacturers would like to see.

“We want to see a more level or fair playing field globally,” says the director of engineering for the manufacturer of pharma, Rx and injectable aseptic products, which operates plants in India and China. “The problem is that overseas facilities are not inspected on a regular basis and domestic facilities are inspected annually. We’d like to have equal inspections for both domestic and foreign markets.”

The scrutiny regarding the lack of offshore FDA inspections is gaining global attention. The Bulk Pharmaceutical Task Force (BPTF) of the Society for Chemical Manufacturers and Affiliates (SOCMA) and the European Fine Chemicals Group (EFCG) of the European Chemical Industry Council (CEFIC)
are calling on the FDA to mandate inspections of foreign active pharmaceutical ingredient (API) manufacturing sites with the cost borne by those sites being inspected. Both organizations have indicated a willingness to pay fees for these inspections when performed on their member-owned facilities that are located outside the United States.

Globalization is Impacting Equipment Purchases

With pharma and medical device manufacturers diversifying their product portfolios, expanding their reach globally and coming under stricter regulations to ensure their products have been packaged and distributed in an error-free environment they are weighing options for sourcing their packaging materials and machinery closer to their manufacturing site.

One emerging trend for why pharma and medical device manufacturers are locating plants offshore is their desire to service emerging markets locally. In the case of one pharma manufacturer that means manufacturing and packaging locally.

When asked to describe the advantages of localized production offshore a senior packaging engineer for a pharmaceutical and medical device manufacturer said: “Better time to market, better feedback, better able to meet regional requirements.”

Figure 10: Equipment purchases, U.S. versus offshore

- In 2008, U.S. OEMs were the dominant supplier of choice. At that time, 58% of companies interviewed said they purchased more frequently from U.S. OEMs, compared to 42% from offshore OEMs.
- In 2012, 3 out of 4 pharmaceutical companies and 2 out of 3 medical device companies operate 50% or more of their equipment from offshore manufactures.

Today, pharma and medical device manufacturers say their intent to purchase the best equipment at the lowest cost is increasing the number of equipment purchases to be made from suppliers outside the U.S.

Even though some companies prefer to work with U.S. suppliers their choice of supplier depends on the type of equipment, the documentation and the cost.

In general, secondary packaging equipment tends to come from U.S. manufacturers, like case packers, palletizers, cartoners and wrapping equipment.
There are specific reasons why manufacturers look to source packaging equipment from offshore machine suppliers and some of those reasons are listed as follows:

- A lot of process equipment comes from Europe. There’s no equivalent supplier in US.
- Offshore suppliers have the filling equipment that U.S. suppliers don’t.
- Only 1 or 2 companies make blister packaging equipment in U.S.
- Offshore suppliers are used for specialty machines and specific applications.
- Critical equipment, like inspection or filling machines comes from Germany or Italy.

A project engineer at a global leader of pharma and OTC products says his firm wants to buy U.S. equipment but doesn’t because U.S. OEMs typically don’t provide the required documentation for their equipment. Nor do they hire validation experts to create validation processes according to FDA requirements.

**Global Shifts in Sourcing Machinery and Materials**

There is a growing preference to purchase equipment from global supplies regardless if they are located in the U.S. or offshore. 40% of pharma and medical device manufacturers said they are attempting to standardize their equipment across all their plants through global sourcing from a single company.

“We try to work with and purchase equipment from local vendors for easier support and flexibility with varied regulations within countries and cultures,” says the senior packaging engineer for pharma manufacturer of biological products and medical devices, such as IV sets and solutions.

The advantage of global sourcing is that manufacturers can use the same equipment in production lines from plant to plant regardless of what country it is located. This allows manufacturers to establish a consistent baseline for machine performance from plant to plant.

One pharma manufacturer said it mandates global sourcing of equipment for primary packaging, such as blister packs, and to a lesser extent, for secondary packaging.

**Figure 11: Equipment sourcing – globally versus locally**

The combined response from pharma and medical device manufacturers interviewed is shown in Figure 11:

- 40% say they source or plan to source equipment globally
- 38% say they source equipment differently from plant to plant due to the challenge of trying to standardize equipment in varied markets

“We are pushing global equipment sourcing if and whenever possible,” says a senior automation engineer for an OTC pharma and medical device manufacturer.
As the push toward globalized sourcing of equipment gains momentum, one hurdle manufacturers need to be aware of, according to a consultant for a pharma packaging firm, is that the number of global packaging OEMs is relatively small, which limits a manufacturer’s choice of suppliers. More suppliers, however, are starting to be established in China and India.

While there are benefits to global sourcing of equipment, pharma and medical device manufacturers interviewed for this report talked about sourcing closer to the point of manufacturing for a variety of reasons and discussed some of the hurdles to overcome with sourcing globally.

Advantages to sourcing according to the needs of the plant are:

- Localized support and service
- Obtain equipment that meets local regulations
- Equipment needs vary plant to plant and are best met locally
- Equipment obtained locally does not have to be imported
- Eliminates electrical differences

Hurdles to watch for when sourcing globally:

- Time differences when dealing with a global supplier can lead to slowdowns in communications about warranty and servicing issues, as well as processing of purchasing orders. For instance, working with a supplier located in a country with a 12 hour time difference can significantly slow communications and tackling of issues that must be handled in real-time can be a problem.

- Language can be a barrier to communications. While English is commonly spoken among business executives interpretation errors will occur in verbal and written communications that can create bumps in the road during design.

- Quality standards for packaging machinery in other countries can vary and in some cases, machine quality and reliability do not meet standards.

- Logistics—the process of getting equipment from point A to point B—should be weighed heavily in any global sourcing relationship. Overseas shipments can get delayed for a variety of reasons before reaching their final destination.

While many of the same advantages and disadvantages to sourcing equipment globally apply to sourcing materials, the leading criteria in making the decision to source globally is primarily driven by cost, availability and quality.
As shown in Figure 12 to the left:

- 23% of pharma and 36% of medical device company’s source materials as close as possible to manufacturing to save on logistic costs and seek out global partners
- Equally, 29% of companies said that suppliers are very specific and only use approved material vendors
- 48% of pharma and 36% of medical device companies say sourcing materials closer to manufacturing is not always possible. In emerging markets there are concerns about material availability and quality.

OEMs looking to fill the global sourcing needs of pharma and medical device manufacturers will be well positioned to win business globally if they take the time to clearly communicate quality standards, minimize logistical issues, provide needed documentation and provide 24/7 availability and support.

**Role of the Contract Manufacturer**

During the past 5 years use of contract manufacturers has increased substantially because they spare manufacturers the up-front capital costs of purchasing new equipment. Among the advantages contract packagers provide are:

- Working out all the bugs in the packaging line in advance of introducing a new product
- Handling custom jobs and product overflow due to smaller batch runs for different SKUs
- Scalability as demand increases

<table>
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<tr>
<th>Percentage of Companies using Offshore FDA-Approved Contract Manufacturers</th>
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<tr>
<td>Pharma</td>
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<tr>
<td>(Mainly Germany)</td>
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<td>Yes</td>
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The advantages of using contract packagers have led to their use by pharma and medical device manufacturers overseas.

- 35% of pharma manufacturers and 21% of medical device manufacturers use offshore FDA-approved contract packagers
- 42% of pharma and 58% of medical device manufacturers do not use offshore contract manufacturers

The equipment engineer at a leading manufacturer of laboratory analyzers said: "If they are selling anything back to U.S. market the contract manufacturers have to be FDA-approved facilities."
III. Packaging Trends and Challenges

Since the FDA announced in late October 2011 that it was considering changes to its pharmaceutical package barcode rule pharma manufacturers have been anticipating what changes, if any, are forthcoming. The FDA’s barcode rule requires manufacturers to put a linear barcode with the National Drug Code (NDC) of the product on most unit-of-use packages.

The FDA’s review of the barcode rule stems from a Presidential order signed earlier in 2011 requiring federal agencies to reevaluate existing rules in order to modernize and strengthen a position on anti-counterfeiting. In response, the FDA elected to reexamine its barcode rule, which went into effect in 2006, as a way to reduce errors when dispensing medications in hospitals.

The intention of the rule was to prevent deaths caused by receiving expired, misbranded or sub potent medications. Requiring the inclusion of a barcode on the medication’s packaging provides hospitals with a way to authenticate, preferably by scanning the barcode at bedside, the drug’s brand, freshness and confirmation that it is the correct medication to dispense.

Since the rule went into effect, more serious concerns about the integrity of pharma products and medical devices being compromised have arisen, the most prominent of which is counterfeiting. In February 2012, counterfeit versions of Avastin, a cancer infusion drug, found its way to physicians and hospitals in the U.S. The case shook the medical profession to its core as it demonstrated that counterfeit drugs were not just limited to pills, as had been previously thought.

The case is expected to prompt the FDA to make changes to its barcode rule to improve protection against phony drugs from finding their way into the hands of unsuspecting medical professionals and pharmacists. One former FDA associate and current president for Center for Medicine in the Public gathered intelligence from government organizations and estimated the market for counterfeit drugs at $75 billion in 2010 and growing by 20% annually.

The Serialization Solution

Serialization requires manufacturers to print a unique serial number on the drug package and link that number to the secondary packaging carton. Individual carton numbers can be linked to the pallet on which the cartons are loaded to enable tracking of the pallet after it leaves the plant. This child-to-parent hierarchy is called aggregation and is one of the leading obstacles delaying serialization implementation.

Potentially complicating the issues around serialization standards is California’s looming 2015 implementation of its e-Pedigree law. The law requires pharma companies to include within the barcode on the package a unique serial number, lot number, and other information to enable tracking and tracing across the supply chain through the use of scanners, software,
and databases. Currently, serial and lot numbers are printed separately on a drug package outside the linear barcode, which contains just a drug's NDC.

In order to fit all the information required by California’s impending e-Pedigree law onto the label, pharma manufacturers must use unique two-dimensional (2D) GS1 Data Matrix barcodes on packages instead of, or in addition to, a linear barcode. If not, there would not be enough space on the label to include all the required information.

Further complicating matters is that other individual states, and the European Union, may impose their own serialization standards. If that happens before a national, and presumably an international standard can be put in place, manufacturers will find themselves navigating a complicated, and most likely, very expensive anti-counterfeiting and product authentication maze.

**An Anticipated Future**

The uncertainty around serialization standards beyond California’s e-Pedigree law has many pharma manufacturers investigating solutions to ramp up development and implementation of track and trace methods they anticipate will meet compliance for any future serialization standards.

“Serialization is a big issue and regulations are coming. Region to region we may be using different track and trace solutions,” says the senior packaging engineer for the pharma manufacturer of biological products and medical devices, such as IV sets and solutions. “We plan to attack the issue to understand the best way to address it and work with FDA.”

But not all manufacturers are as proactive. In fact, some are sitting on the sidelines waiting for the dust to settle before implementing a plan of action or just beginning to test some possible solutions. “Regulatory compliance is unknown. The regulations are changing all the time,” says the director of engineering for the manufacturer of Rx and injectable aseptic products.

**Serialization Bottlenecks**

The pharma and medical manufacturers interviewed shared their concerns about the challenges with serialization that are slowing implementation.

The biggest concern among manufacturers preparing for changes to serialization laws is how to implement a communications infrastructure that aggregates identification of individual units to bundles and bundles to pallets and provide access to the data on how that information is related.

“The communications infrastructure and aggregation is the biggest issue and needs to be addressed as an industry,” says a packaging engineer for a leading pharma and medical device maker. “Aggregation is about following a sequence, and the information has to be accurate. Right now, there are not sufficient solutions available.”
Pharma manufacturers shared their concerns about serialization compliance, listed below in order of significance; all points mentioned are significantly slowing implementation:

- Communication infrastructure and database management issues
- Aggregation – relying on 100% accuracy along the supply chain
- Anticipating FDA regulations and worldwide requirements
- Cost to implement and the manpower it requires
- Having the expertise or finding an experienced full service vendor

Given the uncertainty surrounding serialization, it is not surprising that manufacturers are looking to OEMs to help them find solutions for collecting and aggregating serialized data across the supply chain. “Finding a vendor to provide reliable support for this endeavor is key,” says an engineer for a leading pharma, nutraceutical, medical device manufacturer.

2D Barcodes Lead the Way

For pharma manufacturers the shift from printing linear barcodes to printing serialized 2D Data Matrix barcodes is already underway in order to track and authenticate their products.

The primary reasons manufacturers are embracing 2D barcodes include:

- Low cost of production
- The ability to quickly alter the codes in response to changes in production techniques or when materials come from different suppliers
- Enable manufacturers to quickly pinpoint units that may have problems
- Serial numbers can be included to track an item throughout its entire lifetime, thus making it easier to initiate a recall if needed

In the Figure 13 below, it’s evident that manufacturers are using a combination of solutions to authenticate and track at the unit, case and pallet levels. Clearly, 2D barcodes have become the optimal solution.

Figure 13: A combination of track and trace solutions in use today

In comparison, barcodes were the number one tracking tool used by manufactures interviewed in 2008. RFID tags were predicted to significantly grow in use, followed by non-contact inspection, holograms, color shift ink and covert marking.
In hindsight, manufacturers are not using RFID as widely as predicted 5 years ago because of the high cost at the unit level; however it remains in use at the pallet level for aggregation accuracy. One pharma manufacturer added that holograms are adequate to authenticate products and another said use of non-contact inspection technologies are increasing as a means to check for defective products.

Although 2D barcodes are leading the way as the most practical, cheapest and easiest track and trace solution to implement, a combination of methods is more likely since unit serialization is needed to track and authenticate the product from the beginning to the end of the supply chain. That's why, as one industry expert pointed out, there is no single turn-key serialization solution.

A leading pharma and medical device company, for example, is implementing GTIN (Global Trade Item Number) to specify which manufacturing plant made the medical device using both human readable and 2D barcodes.

Use of non-contact inspection technologies (like camera-readers and x-ray) are increasing significantly to check for defected products, inspect that the proper label is attached and confirm that 2D or covert markings are properly located on the package. A taggant, which is a chemical when added to ink leaves a covert marking, is another solution that was mentioned.

While the cost of integrating serialization and track and trace solutions into the packaging line is a concern for pharma and some medical device manufacturers, they understand serialization standards are inevitable. What they seek from their packaging OEMs are solutions to help meet compliance and guidance on how to implementation those solutions.

**Sustainability – How’s It Going?**

As in 2008, sustainability remains a major initiative for manufacturers as they become more sensitive to the need to reduce packaging waste and use packaging materials that are more eco-friendly.

**Figure 14: Sustainable efforts continue**

As shown in Figure 14 to the left:

- 45% of pharma and medical device manufacturers have launched sustainability initiatives for their packaging
- 13% are not pursuing any changes due to the validation requirements it causes
- 7% are looking for energy efficiencies
- 2% say they have already achieved their sustain goals
Manufacturers in some cases are:

- Using lighter weight materials
- Shrinking the size of their packages to reduce the amount of materials being used
- Moving away from the use of PVC
- Using more recycled and recyclable materials
- Reducing corrugate, whenever possible

One pharma manufacturer is reducing the use of shipping materials by covering bottles loaded onto shipping pallets in stretch wrap, as opposed to placing them in secondary cartons.

“There is a wide variety of sustainable materials, the challenge is making sure the machinery is flexible enough to handle the variety of materials that come in with different specs and different grades,” says the packaging engineer for a pharma, nutraceutical and medical device manufacturer.

Sustainability does not come without its challenges, however. Some of the biggest barriers to embracing sustainable packaging are the increased cost to validate the new material, unexpected material breakages that can occur when using thinner gauge materials that can lead to costly downtime, and the rising cost of sustainable materials.

Manufacturers also noted variances in the quality of sustainable materials that challenge the packaging equipment for primary and secondary packaging. To overcome this problem, manufacturers need packaging equipment that can handle a variety of materials that come in with different specifications and different grades.

Overall, there is a reluctance to change packaging materials if what is being used works properly, since any change in the process would require re-validation and documentation. If the change in material occurs at the end of line primary or secondary packaging, then re-qualification is required.

In short, manufacturers want packaging machinery that can help them balance the increased cost of sustainability efforts with their need to maintain operational efficiency on the packaging line.

**Enhancing Product and Patient Safety**

When it comes to achieving product differentiation, protection and safety there are a multitude of issues manufacturers must take into consideration. For starters, many pharma products and medical devices are sensitive to moisture, oxygen, and light, which if exposure to occurs after leaving the plant floor can degrade their quality. That’s why pharma and medical device manufacturers spend so much time and effort creating a sterile packaging barrier that protects their products.

In addition to product protection, there is also a need for labeling solutions to accommodate the growing amount of information required on pharma and medical device packaging. Some of the solutions include extended labels, packaging inserts and using digital print on demand to be able to make changes quickly.
Finally, pharma manufacturers are wrestling with making sure packages are child-proof while ensuring those who have limited dexterity can open and close the packages properly. Innovations such as squeeze and turn caps on bottles, which were thought to be a better alternative to push and turn caps, did not work well as patients that had trouble gripping the cap due to arthritis or other ailments were unable to open the bottle. Bottom line, the harder manufacturers make it for a child to open a package, the harder they make it for seniors to open the package.

Finding a solution to this balancing act then often requires unscientific measures such as feedback from end-users. It is not uncommon for pharma manufacturers to empanel patients in a roundtable discussion to conduct informal testing of the new packaging solutions and gather opinions on those solutions.

**IV. Machinery of the Future**

As pharma and medical device manufacturers introduce new products it is not uncommon that aging or outdated equipment is incapable of meeting the unique packaging challenges these products present. When that situation arises, manufacturers begin looking at purchasing new equipment.

**Validation**

However, with each new piece of equipment introduced to manufacturing the process must be validated or qualified, which poses a number of complex tasks for manufacturers, including:

- Finding resources internally to do the validation work
- Getting OEMs to provide more validation documentation
- Assessing the risk of achieving a balance between quality, safety and productivity
- The increasing complexity of validating computerized and software controls
- Validating sterile barriers after sterilization
- Validating inspection vision systems

“Having complete documentation on equipment is a challenge,” says a project engineer for a leading pharma company. “We are challenged with accessing risks regarding achieving a balance of quality, safety and productivity.”

In the pharmaceutical and medical device industries, equipment validation is required by the FDA as validation demonstrates that a procedure, process or activity conforms to a written standard. The level of documentation is dictated by the complexity of the system or equipment. The documentation must provide the necessary information and test procedures required to ensure that the system and process meet specified requirements. Hence, systems and equipment must be qualified to ensure good manufacturing practices.
In 2008, the three most frequently mentioned areas of manufacturing where validation remains a challenge remain the same in 2012:

- Product traceability process
- Vision inspection systems
- Online diagnostics

Because one of the biggest challenges facing manufacturers when it comes to validation is finding the time and resources to do it, some manufacturers expressed a desire to have OEMs assist with equipment validation, especially validation of procedures and documentation. They also want OEMs to provide design specifications and support and perform factory acceptance tests (FAT) and installation, operation and performance qualifications (IQ, OQ, PQ).

“It takes too much time to validate,” says a production engineer for a generic pharma manufacturer. “OEMs need to supply factory acceptance test information prior to installation. There needs to be improved validation packages from OEMs.”

The packaging engineer/manufacturing engineer for a maker of ear, nose and throat devices added that validation is minimally a 9 month process for his company. “A lot of time and money has to be spent to get it done,” he added.

One area of the validation process that tends to be overlooked is how it is impacted by sustainability initiatives. As lightweight packaging materials are introduced to the packaging line, manufacturers are discovering they need to perform advance tests to make sure the new materials are compatible with their packaging machinery. In other words, validation must be performed to assure compatibility before a full roll-out of sustainable materials on the packaging line.

“The cost of process validation and regulatory compliance is one of the biggest challenges we face with sustainability efforts,” says a project engineer for an OTC pharma company. “Compliance is the most critical concern because it has to be balanced with operating and machine efficiencies.”

Some of the sustainability initiatives being undertaken by pharma and medical device manufacturers include reducing the use of corrugated by replacing the material with chipboard, improving cubing solutions for packing pallets and thin walling syringes to reduce the material used. Each of those materials must be proven on their packaging equipment.

**Mergers Result in Excess Equipment**

With each expiring patent, pharmaceutical companies face a loss of market share to the makers of generic versions of their drugs. It takes years of research and development, meeting regulatory hurdles and overcoming unforeseen setbacks to bring to market a new, patented medication that can deliver market share gains.
To help maintain market share and obtain more of the resources needed to develop and bring new medications to market faster, many pharma companies are looking to grow their business through mergers and acquisitions. Although helpful from a market share perspective, one of the unintended consequences of mergers and acquisitions is that they have produced a glut of excess equipment. Rather than keep duplicate or unnecessary equipment, the newly merged company will sell it on the secondary market at a cost well below the list price of new machinery.

The growing inventory of used equipment has prompted many pharmaceutical manufacturers to consider purchasing it in lieu of new equipment as a way to hold down costs. When asked if the surplus of used equipment from mergers and acquisitions is causing his company to rethink purchasing new equipment, 45% of pharma companies said yes and 45% said no, as shown in Figure 15 below.

“Why buy new equipment if high quality exists at a discounted price,” says the director of packaging component sourcing for an OTC pharma manufacturer. “Mergers and acquisitions have created an overcapacity of equipment for pharma manufacturers and contract manufacturers to buy used. We are actively selling equipment.”

In comparison, 72% of medical device manufacturers are less inclined to purchase used equipment because they find legacy equipment to be outdated, too difficult to validate or because equipment available on the secondary market does not meet their specific needs. “We always purchase dedicated or customized equipment,” says a manufacturing engineer for a medical device manufacturer of glucose diagnostic strips.

Of the medical device manufacturers interviewed, just 14% said the surplus of used equipment from mergers and acquisitions is causing them to rethink purchasing new equipment.

**Figures 15: Does excess equipment in the market cause a delay in new equipment purchases?**

Despite the preference of many pharma companies to consider used equipment, 45% of the pharma manufacturers opt not to repurpose equipment that comes along with mergers and acquisitions. The reasons cited are similar to those cited by medical device manufacturers, such as it is too expensive to validate or modify used equipment and that legacy equipment bought on the secondary market does not meet the specific needs of their manufacturing line. 72% of medical device manufacturers say they do not purchase used equipment.
Reasons for New Equipment Purchases

New products were cited as the number one reason for new equipment purchases or upgrades by pharma and medical device manufacturers. In comparison, new products ranked as the sixth most common reason for new equipment purchases in 2008.

While the reasons driving new equipment purchases in 2012 and 2008 essentially remain the same, their order of importance has changed somewhat. One significant change is that serialization has now appeared on the 2012 list. It is expected to move up in importance over the next few years.

Figure 16: List of the top reasons for new equipment purchases in 2012 versus 2008

<table>
<thead>
<tr>
<th>2012 Results</th>
<th>2008 Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1 New Product</td>
<td>#1 Higher Output</td>
</tr>
<tr>
<td>#2 Increasing Output/Demand</td>
<td>#2 Increase in Automation</td>
</tr>
<tr>
<td>#3 Replace Aging Equipment</td>
<td>#3 OEE</td>
</tr>
<tr>
<td>#4 OEE</td>
<td>#4 Cost Savings</td>
</tr>
<tr>
<td>#5 Operational Cost Savings</td>
<td>#5 Versatile Changeover</td>
</tr>
<tr>
<td>#6 Meet Compliance Regulations/Validation</td>
<td>#6 New Products</td>
</tr>
<tr>
<td>#8 Serialization/Track &amp; Trace*</td>
<td>#15 Replace Outdated Equipment</td>
</tr>
</tbody>
</table>

Although new products are the primary reason why manufacturers purchase new equipment, the underlying factors of the purchasing decision are more specific. An engineer for a pharma company said that plant consolidation in advance of new product launches in 2014 is driving the company’s need for new equipment.

“We are going to be spending a lot to consolidate facilities for new product launches and equipment procurement is expected to exceed that of preceding years,” says the engineer, who adds 75% of the company’s equipment purchases are sourced in the U.S.

Other reasons cited for why new equipment will be purchased include the increased need for detection systems for solid medicines. Equipment needs will include product sorting, vision systems, laser vision, proximity sensors and illuminant sensors.

A project engineer for a global pharma manufacturer said his company is looking for an optical machine capable of reading labels on round bottles to perform 360° inspection of the bottle. “We are also looking to make modifications to our case packer and palletizing equipment to be able to aggregate from one to another,” he adds.
Plans for New Purchases

When asked about their plans to purchase new equipment within the next 12 to 24 months manufacturers responded as shown in Figure 17 below:

Figure 17: New manufacturing equipment

- 64% of pharma manufacturers and 69% of medical device manufacturers said they expect to purchase new packaging equipment.
- 33% of pharma manufacturers and 19% of medical device manufacturers said they expect to purchase new processing equipment in the next 12 to 24 months and
- 3% of pharma manufacturers and 12% of medical device manufacturers said they have no plans to purchase any new equipment during that period.

“It’s easier to make changes in the packaging end, because new packaging equipment only requires qualification,” says a senior engineer for a pharma and medical device manufacturer. “Validation requirements are for processing equipment.”

New equipment: Are manufacturers spending more or less?

As with any business, pharma and medical device manufacturers have annual operating budgets which allocate funding for new equipment purchases. How much money gets allocated toward new equipment purchases depends on a variety of factors such as:

- Age of existing equipment
- Whether new equipment is needed to accommodate new products
- Whether legacy equipment can be upgraded to effectively extends its useful life

Surprisingly, as shown in Figure 18 on the following page, there was a substantial difference in plans for future equipment purchases between pharma and medical device manufacturers, with 61% of pharma manufacturers planning to increase their equipment purchases in the next 12 to 24 months, compared to just 14% for medical device manufacturers. At the same time, 26% of pharma manufacturers said they planned to spend less on new equipment compared to 36% for medical device manufacturers.
Improving economic conditions was a frequently cited reason among pharma manufacturers and industry consultants for the planned uptick in equipment purchases. “With the economy improving we are losing our fear of investing in new equipment,” says a vice president of packaging technologies for a pharma company. “Companies [in our industry] are sitting on a lot of cash right now.”

Other reasons cited for an increase in equipment purchases include entry into in Latin America and Asia and the need to meet new compliance regulations. The senior packaging engineer for a pharma manufacturer of biological products and medical devices said his firm is undergoing its largest geographic expansion in 30 years, which is driving the need for new equipment.

In contrast, reasons cited why companies are spending less or the same amount in the near future are:

- Large consolidations or major facility upgrades are complete
- Limited number of new drug introductions
- Capital budget constraints
- Excess of used equipment available

One equipment manager for a medical device maker said that his company was not increasing equipment purchases due to a major overhaul of existing manufacturing facilities in 2010. Subsequently, the company’s need for new equipment is less than that prior to the facilities upgrade, he says.

**Aging equipment: To keep it or not to keep it**

Upgrades can extend the life of aging equipment and pharma and medical device manufacturers look to the OEM to support legacy equipment whenever it makes economic sense.

Nevertheless, companies are becoming less inclined to upgrade legacy equipment because of:

- Extensive maintenance needed on outdated machines
- Negative impact on productivity
- Lack of retrofit kits
- Diminishing support from OEMs

In addition, concern about ongoing safety issues as the machine ages is another reason why manufacturers prefer to replace legacy machines with new equipment.

“One of our biggest issues is bringing older machines up to safety standards,” says the packaging engineer for the pharma, nutraceutical and medical device manufacturer. “Our European suppliers do a much better job than U.S. suppliers advising of obsolete equipment and providing a risk assessment on equipment.”
One exception pharma and medical device manufacturers said exists when it comes to replacing legacy equipment with new equipment is when they go through a merger or acquisition. "We try to re-purpose machinery whenever possible before purchasing new," says a senior packaging engineer for a leading pharma and medical device manufacturer.

**What Manufacturers Want in New Equipment**

Just as with many manufacturers in other industries, pharma and medical device manufacturers have specific wants and needs when it comes to new machinery.

As shown in Figure 19 below key areas of where pharma and medical device manufacturers feel OEMs can improve new equipment are:

- Greater flexibility in product changeovers
- Machinery that is easier to clean
- More diagnostics alerts for preventive maintenance
- Machinery that operates at higher speeds to increase throughput and plant efficiency
- Improved operator safety

**Figure 19: Key improvements on the next generation of machinery**

Of the pharma and medical device manufacturers interviewed:

- 50% look to the OEM to support legacy equipment whenever feasible
- 37% replace legacy equipment because it’s too costly to update and validate
- 9% do their own upgrades internally
- 4% bring in a third party when OEMs no longer support aging equipment

*Important to pharma only*
Other key features being sought include more user friendly human machine interfaces, modular design, automation standards, real-time production data, better seal inspection process for thermal inspection and remote connectivity.

In comparison, the top three areas where manufacturers interviewed in 2008 felt OEMs could improve new equipment were:

1. Easy changeover for varied packaging
2. Special modular design
3. Blister pack oriented machines

The emphasis pharma and medical device manufacturers are placing on faster, more flexible changeover is due in part to the increasing number of different SKUs run on a packaging line. One medical device maker said it runs as many as 250 different SKUs through its plant. The more SKUs run on a packaging line, the more changeovers per week involved. The longer the changeover, the more down time and less productivity incurred by the manufacturer.

**Figure 20: Number of SKUs per line now**

While running 250 or more different SKUs on a packaging line is rare, as shown in Figure 20, the number of SKUs per line is expected to increase as manufacturers handle more products on single production and packaging lines to increase operating efficiency. In addition, some pharma and medical device manufacturers are doing smaller product runs to match batch sizes to demand in individual markets.

As a result, pharma and medical manufacturers expect the next generation of packaging machines to perform quick changeover to reduce downtime as the number of SKUs continue to increase.

Along with the predicted rise in SKUs per line come expectations that OEMs will produce flexible packaging machinery that can be changed over ideally in less than an hour.

44% of manufacturers said it takes less than 1 hour and up to 2 hours to complete a changeover. When asked for an acceptable timeframe to complete a changeover on new machinery, 56% of the pharma and medical device manufacturers said less than 1 hour.

Currently 38% of manufacturers interviewed said it takes from 3 to 8 hours to complete a product changeover on the packaging line and that they want to reduce that time to less than an hour.
Of the 12% of manufacturers that said they incur no changeovers, some of the reasons cited included no need for changing the line to accommodate a variation in the strength of the medication and the use of dedicated equipment for specific products.

**Figure 21: Changeover time per line now**

<table>
<thead>
<tr>
<th>Changeover Time</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No changeovers</td>
<td>12%</td>
</tr>
<tr>
<td>Less than an hour</td>
<td>19%</td>
</tr>
<tr>
<td>1-2 hours</td>
<td>25%</td>
</tr>
<tr>
<td>3-5 hours</td>
<td>19%</td>
</tr>
<tr>
<td>6-8 hours</td>
<td>19%</td>
</tr>
<tr>
<td>&gt; 10 hours</td>
<td>6%</td>
</tr>
</tbody>
</table>

**Figure 22: Desired length of changeover time**

<table>
<thead>
<tr>
<th>Changeover Time</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No changeovers</td>
<td>12%</td>
</tr>
<tr>
<td>Less than an hour</td>
<td>56%</td>
</tr>
<tr>
<td>1-2 hours</td>
<td>25%</td>
</tr>
<tr>
<td>4-5 hours</td>
<td>6%</td>
</tr>
</tbody>
</table>

**Modular Design**

While modular equipment design was not a common response to the question about what improvements OEMs can make in their equipment, when asked specifically about it, an overwhelming 72% of pharma and medical device manufacturers expressed strong interest. Of this group, nearly half are already using a modular design which is composed of unit machinery or sections for easy configuration or flexible arrangement.

Primary benefits of modular packaging machinery are that it:

- Breaks down complex machine functions into self-contained processes that increase plant efficiency and flexibility during product changeovers
- Allows for a faster start-up and reduces the machine footprint

“Modular equipment achieves a greater level of flexibility when introducing new products,” says a packaging engineer for a manufacturer of electro surgical devices.

Other advantages of modular design include cost reduction and the ability to customize a machine’s function for a specific need. “There's a lot of interest in modular design for fillers, cartoners and cappers to take up less real estate and do inspection and induction seal in one area,” says the equipment engineer for a leading OTC pharma company.

The engineer for a leading pharma, nutraceutical and medical device manufacturer says his company recently purchased modular machinery made up of 6 modules. “Each module performs a function to complete the entire process, so changes can be easily popped in and out," he says.
Efficiencies from Robotics

The interest in robotics 5 years ago reflects the increased usage of the technology today. In 2008, the majority of companies interviewed expressed interest in adding robotics to their end-of-line packaging. Today an underlying factor driving new equipment purchases is the opportunity to introduce more robotics into the packaging line. Because of the technology’s accuracy in handling materials and ability to repeat the same task faster than human operators, robotics is increasing most frequently on the packaging line. Purposes for which the technology is being used include:

- Placing the product into the package
- Putting the primary package into the secondary package
- Orienting the box on the pallet

“Robotics is an option we are considering more and more and is being used if it makes sense,” says a leading packaging engineer for a pharma, nutraceutical and medical device manufacturer. “Robotics is also being considered for product serialization.”

Still, some manufacturers do not see robotics as a panacea. “Robotics can be tricky in this industry due to quality and control issues, there needs to be an operator to oversee the production,” says the production engineer of a leading generic drug manufacturer.

Figure 23: Robotics is Most Often Used for End-of-Line Packaging

The chart in Figure 23 shows how commonly robotics is being used to bring efficiencies to end-of-line packaging.

- 91% of pharmaceutical companies use or plan to use robotics to improve cartoning, case packing and palletizing
- 71% of medical device companies use or plan to use robotics to improve cartoning, case packing and palletizing

Not to be overlooked is that 29% of medical device companies are looking for more robotics for processing equipment.
Automation Standards
As packaging machinery becomes more automated and capable of capturing real-time analytics to gain better visibility into machine performance during production, manufacturers see a growing need for more machine automation standards.

“Standard communication platforms make it easier to implement network systems,” says an engineer for a pharma manufacturer.

When pharma and medical device manufacturers were asked what kind of operating standards they would like to see implemented in the future on packaging machinery the most common answers were:

- **Control Systems**
  Operating standards for controls can make it possible to develop a set of devices to manage, command, direct or regulate the behavior of other devices.

- **Operating Interface**
  Introducing operating standards for the HMI (human machine interface) helps provide effective control and feedback at the point of human and machine interaction, according to pharma and medical device manufacturers.

- **Safety Systems**
  Standards for safety systems can reduce risk for the machine operator by better protective measures and improve safety at the IO layer, network layer and CPU (central processing unit) layer.

The Need for Real-Time Production Data
The operating standards for automated components will likely aid in the collection of real-time production data.

**Figure 24: The need for data collection to measure machine performance**

In 2008, participating companies predicted that real-time data capture would be achieved in the next 3-5 years as companies move away from detailed line monitoring.

As shown in Figure 24, the prediction 5 years ago has become a reality with 40% of the pharma and medical device manufacturers interviewed today saying they are collecting real-time production data now or moving towards implementation. 29% say it influences their choice in machinery selection.

One advantage of real-time production data is that it can be used for validation and for process standardization, says an equipment procurement engineer at a medical device company.
International symbols preferred but better training is key

Although pharma and medical device manufacturing has become more of a global enterprise, the interest in equipment with bilingual directions or symbols has increased only modestly since 2008. In 2012, 20% of the manufacturers interviewed said it will be important to have bilingual directions or symbols on their next machines, compared to 9% in 2008.

Figure 25: The importance of bilingual direction and symbols on packaging equipment

While the need for bilingual displays is increasing the packaging engineer/manufacturing engineer for the maker of ear, nose and throat devices said that universal symbols would be better.

Several manufacturers said that operator training was the most critical factor in the machine purchasing decision. That’s not surprising given the increasing use of computers and programmable logic controllers in the packaging machinery. The more knowledgeable a machine operator is about the machine, the more efficient he is when it comes to reducing operational errors that can slow production and improving the overall consistency of the packaging line.

“While bilingual directions or symbols would be useful, it is not required; training on the machine is most critical,” says a packaging engineer for a nutraceutical manufacturer.

An engineer for a medical device manufacturer of blood analysis instrumentation concurred, saying: “Operator training is more effective [when it comes to operating a machine] than symbology.”

One alternative to bilingual directions and symbols is the use of international symbols, according to the packaging engineer/manufacturing engineer for the maker of ear, nose and throat devices.

Integrated Packaging Systems

Continuous manufacturing is an emerging trend in pharma production that is opening the door for manufacturers to integrate their production and packaging lines to improve operating efficiencies.

Drug manufacturing has traditionally been a time-consuming process as manufacturers had to mix the raw chemical ingredients that go into the medication in one plant, and then ship the mixture to another plant where it is synthesized into pills, liquids or ointments and packaged. In some cases, manufacturers will add a step to the process by shipping finished product to another plant for packaging.
Because continuous manufacturing creates a non-stop production process that reduces the number of steps required to manufacture a medication, production time for batches alone can be shortened by weeks, and in some cases, months. Integrating the packaging into this non-stop process can further shorten the time it takes to get a product from the plant to the shelf. Further, integrating packaging solutions into the continuous manufacturing process improves packaging quality control as there is continuous end-to-end monitoring of the product.

“There is a huge interest in continuous manufacturing and packaging equipment needs to integrate with the continuous manufacturing processes,” says a project engineer for an OTC pharma manufacturer. “Extruded pills allow for continuous manufacturing and more extended release pills, where one pill a day is taken instead of three a day, is growing in popularity too.”

Implementation of continuous manufacturing processes integrated with the packaging line is likely to require new facility layouts, new product development processes and major changes in the technical skills of the engineers. The complexity of the new system is likely to require a highly skilled operator who understands the entire process, an expert at the Novartis-MIT Center for Continuous Manufacturing said in an article previously published on the subject.

Another factor influencing pharma packaging is myriad regulations governing the production of solid medications, i.e. caplets and chewables, vs. those for liquid medications. An equipment engineer for a leading pharma manufacturer says plant production is now specialized to accommodate either solids or liquids.

“There are too many regulations that make it too expensive to switch back and forth from solids to liquids and vice versa,” he says.

V: Conclusion – A Vision of the Future

Without question, manufacturer’s equipment needs are substantially changing due to:

- The increasing diversity of pharma products and medical devices
- The globalization of production and packaging
- The regulations that govern both industries

For pharma manufacturers in particular, many of those changes have occurred in the past 5 years. In 2008, manufacturers expressed no need for packaging equipment that comes with validation documentation. Today that specification ranks high on their list of purchasing criteria for new equipment.
Track and trace needs have also undergone significant changes. Today, 73% of pharma and medical device manufacturers say that 2D barcodes are expected to be part of any track and trace solution they develop. In 2008, 2D barcodes were not even on their radar. At the same time, RFID technology, which was thought to be a backbone technology for track and trace solutions going forward, is losing favor due to its high cost of implementation. Meanwhile stacked linear barcodes, UV markings and taggants, which were also not on manufacturer’s radar in 2008, are among the technologies manufacturers are considering for use in their track and trace solutions today.

The uncertainty around serialization standards beyond California’s e-Pedigree law is also clouding the horizon for pharma and medical device manufacturers when it comes to their packaging machinery needs. Without a clear picture of how the regulatory landscape will shake out on this issue, not only in the U.S., but globally, manufacturers are likely to be looking to a third-party that can help them plan for the future.

As a result, pharma and medical device manufacturers are looking to OEMs for new equipment to help keep pace with the rapid changes taking place in the industry when it comes to product packaging. For OEMs that means delivering equipment and solutions that provide manufacturers with consistency of operations across all their plants globally and machine performance analytics that can be integrated in to back office systems for company-wide access. In addition, manufacturers expect OEMs to build equipment that is compatible not only with FDA regulations, but international quality and consumer safety standards.

Just as in other packaged goods industries, pharma and medical device manufacturers expect OEMs to be partners; a company they can rely on to guide them on how best to set up packaging lines to help them when it comes to impending serialization laws and regulations and provide equipment that increases operating efficiency and plant productivity.

By taking the time to understand the issues impacting pharma and medical device manufacturer’s business OEMs can provide the equipment solutions that not only wring more efficiency out of the packaging line, but ensure their clients meet complex and evolving compliance regulations.
Actionable Check List
End users most critical concerns that machine builders need to know

#1  Build Easier to Use Machines
   Flexible
   Quick and efficient changeovers
   Intuitive diagnostics and operator interface
   Cleanable
   Efficient
   Reliable
   Operator safety

#2  Understand the Complexities of Validation
   Assist with equipment validation
   Supply documentation
   GMP - Good Manufacturing Practices
   FAT – IQ – OQ – PQ

#3  Be a Partner
   Visit the manufacturing facility
   Understand the need for specialized equipment
   Amicable to the changes needed

#4  Support Aging Equipment
   Recommend equipment improvements
   Smarter components and communications
   Parts availability
   Safety standards
“The cost of process validation and equipment qualification is one of the biggest challenges we face.”

Production Engineer
Appendix A

Industry Participants

The findings in PMMI’s *Pharmaceutical and Medical Device Industry Segment Report* are based on 50 conversations with pharmaceutical and medical device manufacturers, contract manufacturers/packagers, and industry experts working on serialization, validation and industry compliance.

**Figure 26: Segmentation and titles of survey participants**

![Diagram showing segmentation and titles of survey participants]

**Industry Ranking**

Of the 48% of participants in the pharmaceutical industry interviews included:

- 8 out of the top 10 ranked pharma companies
- 5 out of the top 10 ranked generic companies

Pharmaceutical companies that manufacture pills, capsules, tablets, patches, inhalables, injectables, vaccines, OTC, generic, nutraceuticals and animal health products

Of the 30% of participants in the medical device industry surveys were conducted with:

- 8 out of the top 10 ranked medical device companies

Medical device companies that produce testing equipment, surgical kits, cell analyzers, lab instrumentation, diagnostic devices, orthopedic implants, surgical implants and disposables
Appendix B

References and Resources


googoleimages.com


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