HEALTH SCIENCES

ERNST & YOUNG

Quality In Everything We Do

Coming and Going

What's Really Going on in Your Global Supply Chain?

What's Really Going on in Your Global Supply Chain?

As the incidence of counterfeit and diverted drugs grows, leading pharmaceutical companies around the globe are taking steps to enhance the integrity of the supply chain—because nothing less than the good name of their organizations and the public health is at risk.

Globalization of the pharmaceutical supply chain, technology advancements, and growing price disparities between markets are causing significant shifts in the flow of medicines. Whether it is the legal re-sale of products among U.S. wholesaler-distributors via parallel traders in member countries of the European Union (E.U.), or the illegal flow of genuine or fake pharmaceuticals from emerging markets to the United States and other developed countries, the integrity of life-saving and life-enhancing medicines is increasingly uncertain.

Public trust in the pharmaceutical supply is paramount. Executives are searching for ways to address problems associated with the diversion, theft, and counterfeiting of pharmaceuticals.

According to the Pharmaceutical Security Institute (PSI), the total value of counterfeit, diverted, and stolen drugs in 2003 increased sevenfold over amounts reported in 2002. Worldwide, 363 people were arrested in 2003; the average value of seizures was $3 million, according to PSI. The U.S. Food and Drug Administration (FDA) says that counterfeit

> "This is a thoroughly regulated industry in the United States, from the manufacturer to the pharmacist. The question is, 'If there is such a tight system, how in fact does this occur?' The answer is that there is an element of criminal conduct and a high value in moving into this [counterfeit] market."
>
> Thomas Kubic, Pharmaceutical Security Institute.
> Source: Ernst & Young Roundtable November 12, 2004.

drugs comprise 10 percent of worldwide market and generate revenue of $32 billion.

In 2004, the incidence of theft, diversion, and counterfeiting increased by 16 percent to 553, according to the PSI.

Source: Pharmaceutical Security Institute, 2004

The pharmaceutical supply chain's evolution and the changing regulatory environment are raising new concerns. Historically, a top priority was to streamline the process and eliminate inefficiencies. Today, the pharma sector boasts one of the most efficient supply chains relative to other sectors. Nonetheless, while manufacturers, wholesaler-distributors, and pharmacies work to achieve cost-savings, a major focus is addressing the increase of counterfeit drugs in the supply chain worldwide, and the increasing number of law suits being lodged against each of the key stakeholders.

Increasingly, "an array of operational and technological solutions are at hand to ensure the integrity of the global pharmaceutical supply chain and to make sure that the right drugs reach the right patient in the right place," says Jeff Steinberg, a partner at Ernst & Young. "In many cases, best practices used in other industries such as consumer goods and information technology are being tailored for the pharmaceutical sector with great success," Steinberg notes.

A Global Challenge

As manufacturers, wholesaler-distributors, and retail pharmacies try to deliver on their promises to a geographically diverse customer base, the need grows for control along the global supply chain in almost every direction. The path from the lab to clinical trials to manufacturing and distribution can stretch for thousands of miles across oceans and borders. For Internet pharmacies in particular, borders have become largely irrelevant.

By any account, the number of counterfeit drugs is increasing globally. Interpol estimates that 5–7 percent of drugs worldwide are diverted or counterfeit. In 2004, the incidence of theft,

"The prescription drug counterfeiting business has become a highly sophisticated, globalized endeavor, encompassing highly specialized distribution syndicates that deliver high-quality replicas of packages containing counterfeit drug product."

D. W. Howell, Director of Global Product Protection, Eli Lilly and Company.
Source: Testimony before the Health and Human Services' Task Force on Drug Importation, April 5, 2004.

diversion, and counterfeiting increased by 16 percent to 553, according to the PSI. In 2004, the FDA initiated nearly 60 counterfeit drug investigations, a two-fold increase over 2003. Pharmaceuticals in every therapeutic category are targets of criminal activity. According to the PSI, 590 different products were involved in the 553 incidents occurring in 2004.

Long considered a problem in developing countries where the World Health Organization (WHO) estimates that 25 percent of drugs are counterfeit, the growth of cases in the United States and Europe has gripped the attention of industry, policy makers, and the public alike. Anti-counterfeiting activities are a top priority for an array of industry associations and regulatory agencies, and new regulations are being implemented worldwide to enhance security.

> **"The bottom line is greed and money and as long as there's a huge profit margin and a small risk, this will mushroom."**
>
> Thomas Kubic, Pharmaceutical Security Institute.
> Source: Pharmaceutical Security Institute, 2004.

Myriad factors contribute to the current trend in pharmaceutical diversion and counterfeiting, including:

- Significant price differentials between markets, coupled with price-sensitive consumers looking for lower-cost sources of medication
- Pressure on company margins and employee compensation that creates financial incentives to divert product or engage in counterfeiting operations
- Sophisticated technology that renders counterfeit products nearly indistinguishable from branded originals and a lack of knowledge and training on spotting and reporting suspicious products
- Difficulties in adequately monitoring the compliance of third-party vendors once they assume or re-assume control of products at various points along the supply chain
- Prohibitions in some markets to impede the re-sale of product across borders, which may involve repackaging, from lower-cost to higher-cost countries
- A shortage of resources to support customs, border protection, and inspection sites
- A lack of communication between wholesaler-distributors, manufacturers, and retail pharmacies

- An inability to verify the integrity and compliance practices of Internet-based pharmacies

As these trends continue, the opportunity for business and safety risks will increase. As a result, manufacturers, wholesaler-distributors, and pharmacies are increasingly utilizing an enterprise-wide view of their supply chains. As wholesaler-distributors work to demonstrate their value to manufacturers, they know that certifying the integrity of their operations will become increasingly important as a competitive advantage in the market.

Technology: Aiding and Abetting

Technology has become a doubled-edged sword for the pharma industry. It has allowed companies to achieve significant efficiencies in manufacturing processes to reduce costs. The increasing adoption of radio frequency identification (RFID) technology, which enables track-and-trace capability for pharmaceuticals in the supply chain and is a replacement for bar codes, will increase security and operational efficiencies.

Stakeholders are optimistic that electronic product codes (EPCs), which are stored in an RFID tag, will serve as an effective anti-counterfeiting tool. Many large pharmaceutical companies and wholesaler-distributors already are in the process of evaluating EPC technology, which identifies the product and gives a unique product number to each box, case, or bottle. Widespread adoption of this technology will take time, impose additional costs, and raise data privacy concerns that the industry must work to address.

Increased collaboration by key stakeholders in the supply chain also will be necessary to achieve the intended benefits of EPC and RFID solutions. Ultimately, even with widespread adoption of new technology, opportunities for counterfeits to appear will continue, given the complexity of the supply chain and the number of players involved.

Manufacturers, wholesaler-distributors, and pharmacies are testing the waters with RFID and EPC technology. Two pharmaceutical manufacturers with products at high risk for counterfeiting and diversion, Pfizer and Purdue Pharma, recently committed to investing millions of dollars to conduct a pilot program to integrate unique RFID tags on drug labels.

In the United States, the FDA is recommending that all manufacturers adopt RFID and EPC technologies by 2007. Many manufacturers, wholesaler-distributors,

chain drug stores, and retailers are expected to begin implementing these technologies in 2005 and 2006. Still unknown, however, is how regulatory agencies will monitor the use of these systems, and what companies will be required to do in order to validate their compliance.

Increased use of anti-tampering or tamper-evident technologies also will help curb the incidence of patient encounters with counterfeit drugs. Many new technologies—from holograms to unit-of-use packaging—can serve as tools that stakeholders can use in conjunction with other actions to help protect the integrity of products.

But along with the increased benefits of technology come risks. Criminals are using new technology to replicate legitimate packaging, making counterfeit drugs indistinguishable from the true product. The Internet provides easy access to the tools and equipment necessary to manufacture and package counterfeit drugs, and to retain the anonymity that allows them to continue selling and distributing drugs in today's global, E-commerce environment.

Staying one step ahead of criminal activities is challenging, but not impossible. While on the one hand technology facilitates the counterfeit drug trade, it also assists forensic professionals in tracing the source and destination of counterfeits. Technology alone, however, is unlikely to protect the supply chain. This point was underscored by the FDA in a February 2004 report, *Combating Counterfeit Drugs*.

Regional Distinctions

Though illegal diversion, theft, and counterfeiting are global in scope, implementation of anti-counterfeiting measures can be regional and local. Regions, as well as individual countries may require a unique approach to enhancing supply chain integrity, given differences in the composition of the supply chain, laws and regulations, and the commitment of law enforcement to crack down on counterfeiting, theft, and diversion.

Europe and Parallel Trade

Parallel trade involves the legal re-sale and re-packaging of products sold in one country and delivered to the end-user in another. The practice is thriving in the E.U., in which a single approval by the European Medicines Agency (EMEA) allows for the free flow of medicines across E.U. member-state borders. E.U. laws and judicial decisions support the free flow of goods among the member states; the aim is to create a single market for pharmaceuticals and other goods in the region.

Because pharmaceutical prices vary from one market to another in the E.U., profits can be made simply by moving drugs from

a lower-priced country to a higher-priced environment. Article 81 EC (anti-competitive agreements) and Article 82 EC (abuses of a dominant position) restrict manufacturers from inhibiting the re-sale of pharmaceuticals via wholesaler-distributors and third parties (parallel traders) created specifically to conduct arbitrage in this market. An estimated 140 million drug products are parallel-traded annually in the E.U.

The integrity of the supply chain and manufacturers is of great concern because of the:

- Inability to prevent shortages of drugs in lower-priced countries
- Difficulty in conducting efficient recalls of adulterated product
- Possibility for counterfeit drugs to enter the supply chain as products pass through multiple organizations, some of which lack proper security controls or discard anti-tampering technology

The accession of new member states to the E.U., particularly those bordering Russia (which is known to have a high incidence of counterfeit drugs), increases the risk that the integrity of the supply chain will be compromised.

The WHO was quoted in the U.K.'s *The Independent* in January 2004, stating that the accession of the new member states "will make the E.U. even more vulnerable to the global trade in illegal pharmaceutical drugs."

But counterfeiting is not confined to emerging markets in the expanded Europe. In November 2004, police in the U.K. uncovered one of Europe's largest counterfeit manufacturing operations, able to produce more than half a million fake pills daily. Authorities found fake Viagra®, diazepam, and anabolic steroids valued at more than $11 million. The head of the operation, a former pharmaceutical sales representative with basic chemistry qualifications, was importing chemical supplies from India.

The options that manufacturers currently have at their disposal to enhance the integrity of the supply chain are limited by the legal restrictions currently in place. Competition law prevents:

- Manufacturers from using intellectual property (IP) rights to prevent parallel trade between E.U.-member countries
- Agreements between businesses to inhibit E.U. parallel trade

- Manufacturers with a dominant market position from acting to inhibit E.U. parallel trade

"However, the legal environment is constantly evolving," says Patrick Flochel, Ernst & Young European Pharmaceutical Leader, "and manufacturers may have greater flexibility in the future to track the flow of their product throughout the region."

In the meantime, executives are considering different ways to restructure their distribution systems to improve the likelihood that their products are reaching the patients for whom they are intended.

North America and Reimportation

The question of whether the U.S. government should allow pharmaceuticals to be imported from Canada, and perhaps other developed countries, is at the center of ongoing and intense debate. The outcome of the debate will have repercussions for the pharmaceutical supply chain.

Manufacturers are taking direct actions in North America to curb the flow of products across the U.S.-Canadian border. First, some manufacturers have restricted shipments of products to certain Canadian wholesaler-distributors and retail pharmacies if they are known to export products to the United States. Second, some manufacturers are engaging third parties to audit the compliance of wholesaler-distributors with the terms of trade included in their contracts.

Meanwhile, various state and city governments are fueling greater reimportation by establishing programs to purchase pharmaceuticals from Canada for their employees. Despite its reservations, the federal government is tacitly allowing these programs to operate for the time being.

Among the proactive steps industry executives can consider to enhance the integrity of the supply chain are:

- Perform supply-chain audits in the United States and Canada
- Review and revise contract terms of trade
- Establish or enhance internal brand protection programs
- Adopt track-and-trace, unit-of-use anti-tampering technology
- Employ forensic IT tracing in instances where Internet sales with unknown origins are suspected
- Consider conducting covert sting operations to detect counterfeit or diverted drugs

- Develop compensation and reward incentives for employees that discourage diversion
- Leverage applicable customs and anti-terrorist regulations to protect intellectual property and safeguard the supply chain
- Re-evaluate company procedures for acceptance of returned product and the use of a third party to handle returns for the company
- Consider the impact of new legislation and regulation on a national, state, and local level

Canada remains the focus in many of the discussions about reimportation. But many of the concerns relate more directly to those countries that are supplying Canada, or would have the incentive to supply Canada, with enough products to meet the sky-high demand from U.S. consumers now and in the future, should reimportation become legal.

Manufacturers may see some hope emerging at the state level. Florida, for example, passed a law requiring a paper pedigree for all wholesaler-distributors of prescription drugs as of July 1, 2006. Meanwhile, wholesaler-distributors selling drugs included on a "specified drug list" to another wholesaler must immediately follow paper pedigree requirements. Separate pedigree requirements are in place for wholesaler-to-wholesaler sales of drugs not included on the list. The new requirements are viewed by some as the tip of the regulatory iceberg of state efforts to oversee wholesaler-distributor traffic.

Asia-Pacific

The pharmaceutical industry and U.S. FDA officials are increasingly concerned about the risks posed by counterfeit drugs and raw materials that are emanating from Asia and, in particular, from China.

The Pharmaceutical Research and Manufacturers Association (PhRMA) estimates that upwards of 10-15 percent of annual industry revenue is lost to counterfeiting in China. The association says that counterfeit activity in China is on the increase, evidenced by the growing number of counterfeit drugs discovered in Chinese domestic and international airports.

The lack of effective legal and regulatory deterrents to counterfeiting is cited as a key reason for the problem, and enforcement activities remain insufficient. China's entry into the World Trade Organization (WTO) has spurred greater collaboration with industry in the crackdown on counterfeits. One major pharmaceutical company worked with Chinese authorities to carry out seven raids on

counterfeiters, which resulted in the seizure of $8 million worth of products.

The appearance of counterfeit drugs in Hong Kong in 2003 increased concern in the region, given the high regulatory standards in place in that country. According to the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), patients in Southeast Asia have a one in ten chance of purchasing a counterfeit drug. In China, authorities estimate that the average percentage of counterfeit copies may reach 50 percent for some products, according to IFPMA.

Products found in circulation in China and other emerging Asian countries tend to be more common drugs such as penicillin, whereas the lifestyle drugs produced in these countries are destined for developed countries.

In response, pharmaceutical companies are taking a proactive approach to reduce the production and distribution of counterfeits. Companies also work under the auspices of the Quality Brands Protection Committee in China, which conducts market sampling and surveillance, as well as raids on suspected counterfeit manufacturers and distributors.

Malaysia's Ministry of Health is stepping up its efforts to prevent counterfeit imports and manufacturing by establishing a directive on the use of the hologram security device. Effective in 2005, the regulation requires each unit of sale for pharmaceuticals (except those requiring cold chain maintenance), health supplements, and over-the-counter products to bear a hologram security label. A unique serial number in the label will verify that the product has been registered with Malaysia's Drug Control Authority (DCA) and can be traced to the licensed manufacturer or importer of the product.

In 2003, Chinese officials uncovered $60 million worth of counterfeit drugs and destroyed 994 manufacturing or distributing facilities.

Source: Ernst & Young analysis, 2004.

Singapore has taken action by modifying parallel importation rules for pharmaceutical products. Recent regulation allows patent owners to stop a parallel importer from importing a product that is a generic equivalent or similar to a patented product if the product has not been previously sold or distributed in Singapore. Once the patent owner imports the product into Singapore, however, it will lose that right and the patent owner can be subject to competition from parallel importers. In order to balance the rights of the patent owner and barriers to access, a product may be parallel-imported with the government's

approval if a patient requires the medicine and there is no alternative drug on the market.

Seeing is Believing

Transparency is essential to ensuring the integrity of the supply chain, and maintaining the trust of vendors, business customers and, ultimately, patients. At Ernst & Young, we see this trend occurring not just in regard to the supply chain, but in all facets of operations as companies work to demonstrate accountability, rebuild trust, protect brand reputation, and mitigate risks.

So what are the implications of this trend as it relates to the pharmaceutical supply chain? Areas in which various stakeholders—from government to manufacturers to patients—are looking for greater clarity include:

- Product pedigree—Who controls the product along the supply chain?
- Licensure—Where can stakeholders see the licensing requirements for manufacturers, wholesaler-distributors, and pharmacies? Who is in compliance with those requirements?
- Contracts—How can stakeholders verify that third-party vendors are complying with promises made in their contracts?
- Internal controls—What standard operating procedures are in place within each company to help monitor the safety and integrity of the drug as it passes through its hands?
- Enforcement—Who do we contact first if we identify suspicious products? Who has ultimate authority for a given jurisdiction?
- Intellectual property (IP) – How can pharmaceutical companies successfully perform in markets where IP rights are not always upheld?

Certain manufacturers and primary wholesalers have begun asking the right questions. They have instituted change in their own supply chain, beginning with their link with wholesaler-distributors. This change is coming about because of the widespread gray market that exists within the large and diffuse wholesaler industry, whereby products may pass through the hands of multiple wholesaler-distributors before reaching their final destination, and thereby expose the supply chain to counterfeits.

There is not yet one standard approach in the industry to curb sales in the gray market. Indeed, manufacturers' first steps have involved a variety of new restrictions incorporated into revised terms of trade with wholesalers that are purchasing their product. The relative intensity of new requirements varies. Some

contracts mandate that wholesaler-distributors only buy directly from the manufacturer, while others allow wholesaler-distributors to purchase directly or from other wholesaler-distributors on a list of manufacturer-approved companies. In the case of the former, laws and regulations requiring a paper or electronic pedigree are less meaningful. In the latter, a pedigree requirement may help wholesaler-distributors uphold the integrity of the supply chain.

While manufacturers increasingly are aware of the dangers posed by the circulation of their product in the gray market, new weaknesses in the supply chain are emerging. For example, wholesaler-distributors are regularly accepting returns of products despite not having sold the product to the end user. Wholesaler-distributors may have a financial incentive to re-sell the product, assuming the product is not damaged or short-dated, to other wholesaler-distributors or retail pharmacies. In some cases, wholesaler-distributors lack rules or guidelines for employees on how to handle returns, including whether or not they are expected to check the drug's pedigree prior to re-stocking the product.

"Controls over purchased product are in place in general, but controls over returned product are still somewhat lax. This opens a window of opportunity for counterfeit or adulterated drugs to enter the supply chain," Jeff Steinberg maintains.

Moreover, wholesaler-distributors sometimes rely on third parties to handle returns of damaged and short-dated drugs from their customers. The involvement of a third-party returns processor adds yet another layer of vulnerability to the supply chain. Without proper controls to certify the integrity of returned products, these organizations open another window of opportunity for adulterated or counterfeit products to enter the supply chain.

Ernst & Young has found that while some strategies can be applied in various theaters, careful consideration of regional, national, and local regulations, laws, and business practices is necessary to optimize the opportunities for success. For large multinational companies, this task is challenging.

In instances in which a company's brand name is being externally leveraged for financial gain, increasing the likelihood of product and company brand damage, corporate investigations work well in the pharmaceutical industry. An ounce of prevention in many cases costs far less than the potential impact of a counterfeiting event.

Action Steps

Ernst & Young has found through its compliance work with clients that taking control of the situation means that a company—be it a manufacturer, wholesaler, or distributor—must take a holistic view of

the problem. For the company's brand, its intellectual property rights, its legal liability, and its margins, the potential financial impact of a case of counterfeit or diverted products bearing its brand name can be significant. However, estimating that cost can be difficult, making it hard for companies to gauge the right amount to invest in order to mitigate the risks sufficiently.

Executives can ask the following questions to begin thinking about the likelihood that their products will be diverted or counterfeited, the potential harm that may cause, and whether they are currently taking steps necessary to mitigate those risks:

- Which, if any, of our brand-name products sell at significantly different prices in markets around the world?

- What kind of mechanism does our company have in place to determine whether or not our products are diverted from their original destination? How do we know how well that system is working?

- Are the regulations and safeguards in emerging markets adequate to safeguard the integrity of our product?

- What are the potential safety risks posed for patients who may receive a diluted formulation of our product?

- Do we have minimum inspection standards in place for returns being restocked for resale?

About the Business Risk Services Group

The Ernst & Young Business Risk Services team designs client-tailored approaches to conduct site visits with wholesalers and distributors to assess their internal procedures and controls, audit compliance with manufacturers' required conditions of sale, and provide recommendations as necessary to improve the integrity of the manufacturer's supply chain. The scope of the engagement can vary from regulatory and legal assessment of the current environment, to devising appropriate terms and conditions of sale, to full-scale audits of wholesalers to help ascertain the integrity of the supply chain from beginning to end.

About Ernst & Young

Ernst & Young, a global leader in professional services, is committed to restoring the public's trust in professional services firms and in the quality of financial reporting. Its 100,000 people in 140 countries around the globe pursue the highest levels of integrity, quality, and professionalism to provide clients with solutions based on financial, transactional, and risk-management knowledge in Ernst & Young's core services of Audit, Tax, and Transaction Advisory Services. Further information about Ernst & Young and its approach to a variety of business issues can be found at www.ey.com/perspectives. Ernst & Young refers to all the members of the global Ernst & Young organization.

For more information you may contact:

Jeff Steinberg, Partner
Business Risk Services
jeffrey.steinberg@ey.com
(212) 773-2232

Patrick Flochel, Partner
European Pharmaceuticals Leader
patrick.flochel@ch.ey.com
+41 58 286 41 48.

Case Study

Ernst & Young was retained by a pharmaceutical company (Company X) based in a Southeast Asian country. Officials at Company X had discovered that a quantity of their drugs were being counterfeited and sold over the Internet. The company wanted to shut down the illicit operation before it impacted its financial position and its brand reputation

Ernst & Young's goals were to:

- Establish the identify of any person(s) involved in the online distribution of Company X's products
- Identify the name, location, and involvement of any illicit laboratory producing counterfeit products
- Provide advice and support to terminate the production and force the closure of any such laboratory

Through computer forensic inquiries and background searches, Ernst &Young professionals were able to identify a number of addresses and individuals involved in the activity. Through site visits to verified addresses, on-site interviews, and surveillance, Ernst & Young was able to confirm the illegal manufacturing operations and identify the individuals responsible. Company X reported the information to the police, who arrested the individuals and shut down the illicit manufacturing operation.

Source: Ernst & Young

Ernst & Young

ey.com/us/pharma

SCORE Retrieval File
EYG No. CW0001