U.S. PHARMACEUTICAL AND MEDICAL DEVICE MANUFACTURERS:

Supply Chain Trends and Canadian Cross Border Efficiencies

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Introduction

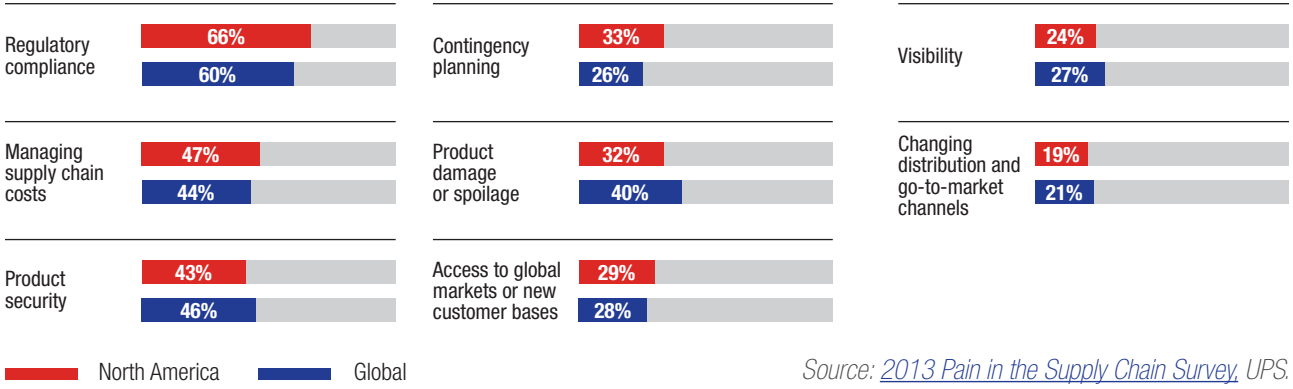
A health products logistics supervisor found himself faced with a "perfect storm" of challenges not long ago: A critically-important product in need of delivery to a rural hospital, a major ice storm, and no carrier availability. Well-trained in the life-and-death nature of healthcare-related logistics, the supervisor jumped in his own vehicle and made the delivery himself. This example, which was highlighted in an International Warehouse Logistics Association publication, highlights the unique challenges inherent to healthcare-based supply chains.

While every business understands the pressure of tight delivery schedules and production efficiency, few operate under the same life-and-death circumstances as healthcare product manufacturers. Both medical device and pharmaceutical manufacturers face unmatched pressures for product quality and on-time deliveries. And both face numerous external factors that are fundamentally changing the scope of their industries, and forcing changes in traditional supply chain practices.

Among the key trends currently affecting how healthcare products are manufactured and distributed:

Regulation and Compliance. Without a doubt, increased government oversight is a constant source of angst for healthcare manufacturers. Recent research found "for the third consecutive year, regulatory compliance is the top supply chain pain point" for healthcare executives. U.S. manufacturers must contend with growing numbers of regulations from the U.S. Food and Drug Administration (FDA), including the "Drug Supply Chain Security Act" which will be phased in over the next ten years. Businesses that ship to Canada must contend with Health Canada regulations, and global distributors face a patchwork approach to regulatory compliance, with each country maintaining its own medical device and pharmaceutical regulations.

SURVEY PARTICIPANTS CITED THE FOLLOWING SUPPLY CHAIN ISSUES AS CONCERNS



Source: 2013 Pain in the Supply Chain Survey, UPS.

Soaring Demand. A combination of an aging population and an increasingly global marketplace has increased demand on manufacturers. Another consideration is the U.S. Affordable Care Act, which is intended to offer health insurance to millions of previously under insured and uninsured individuals. Not only do manufacturers face increased demand for existing products, but also pressure for more efficient treatments and solutions for illnesses and physical ailments.

Shifting Customer Needs. As research and technology continue to fundamentally transform healthcare capabilities, the supply chain is being forced to adapt to changes in the types of products brought to market. For example, the use of injectable cancer treatments has increased by 20 percent in recent years, while bioengineered vaccines are expected to account for 23 percent of the global market by 2016, up from 17 percent during 2009. Another consideration is the change in the way healthcare is being administered. Patients are increasingly turning to home healthcare solutions,
or flocking to local urgent care clinics, which has resulted in a need to find ways to deliver medicines and supplies to homes and non-hospital medical facilities.

Surge in Generic Drugs. Generic drugs accounted for 84 percent of all prescription medications during 2012, and is expected to account for 87 percent by 2017. Fueling this growth have been patent expirations for many top-selling, and highly profitable drugs. This trend in patent expirations, known as the "patent cliff" is expected to continue through 2018.

But with these challenges come opportunities, and healthcare manufacturers are increasingly recognizing the need to reevaluate supply chain operations to reflect the changes taking place. State of the art facilities are able to ensure proper handling ranging from temperature control, storage, security issues and inventory management. Customized transportation solutions can ensure a logistics plan that meets businesses precise needs, with flexibility to adjust to last minute changes and the inevitable supply chain "emergency."

Choosing the right logistics partner is one of the most important decisions a medical device or pharmaceutical supply chain manager will make. In an industry that can tolerate a zero percent margin of error, a manufacturer must choose an experienced logistics provider with the necessary capabilities. Can the logistics provider guarantee the specialized warehousing and transportation needs your products need? Does the provider have capability to reach your customers without having to transfer shipments to another truck – even another carrier? Can the carrier document its experience and effectiveness in managing the U.S. compliance process? What about shipments to Canada? Does the carrier have a distribution system to reach your Canadian customers, and ensure full compliance with Health Canada and the Canada Border Services Agency?

Few industries face the scrutiny and demand for excellence as those engaged in healthcare product manufacture. As the following discussion will make clear, it is a time of transition within the industry, but also an opportunity to attain tremendous improvement in supply chain performance.

Challenges to the Health Products Supply Chain

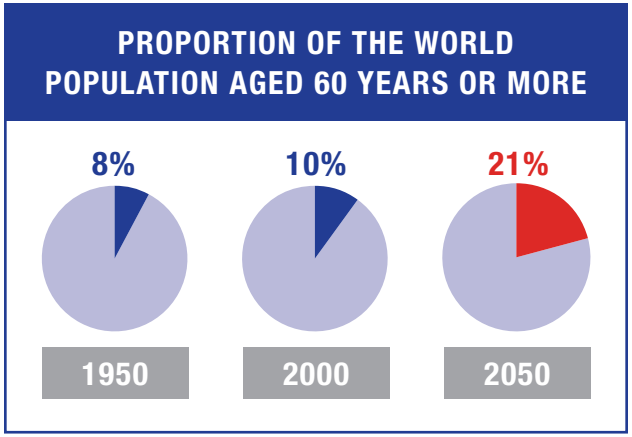
"Anyone in healthcare who feels totally satisfied or relaxed is not paying attention," George Barrett, chairman and CEO of Cardinal Health, Inc. said in a KPMG study on the business regulatory environment. "Between the regulatory and legislative changes and the simple realities of our national health, both economic and physical, it is clear that healthcare will change."

What specifically are the "simple realities" and the regulatory and legislative changes to which Barrett refers?

In fact, several key drivers have taken hold within the healthcare industry, and are impacting most every aspect of the manufacture and delivery of healthcare products, including pharmaceuticals and medical devices. New legislative mandates in the Affordable Health Care Act, will potentially add tens of millions of new patients into the U.S. healthcare system, thereby increasing demand for medicines and devices. In addition, the Act's 2.3 percent medical device tax, could result in higher consumer prices. Another factor is the FDA's "Drug Supply Chain Security Act," intended to manage risk in the pharmaceutical supply chain by establishing, over the next ten years, an electronic tracing system of pharmaceutical products, down to the package level.

Demographic Factors

The aging of the population is increasing the number of patients in need of medicines and devices. According to research published in the International Journal of Epidemiology, the number of Americans aged 85 or over, which is the group most likely to need long-term healthcare services, is expected to increase by 350 percent during the 2000-2050 period. Cardinal Health's Barrett noted that 10,000 people per day become eligible for Medicare, "many suffering from at least one chronic illness."



Source: SupplyChainBrain, Sept/Oct 2014.

The surge in demand for healthcare services has led to a fundamental change in the manner in which patients receive services, notably an increase in new venues in which services are offered – private homes, community centers, retirement homes, retail stores, mobile clinics, urgent care clinics and physicians' offices. This is in addition to traditional

distribution venues including hospitals, clinics and pharmacies. Manufacturers must broaden distribution channels to ensure that supplies are delivered to each of these "new" venues.

The aging of the population is not unique to the United States, and the result has been an increased demand worldwide for pharmaceuticals and medical devices. China, for example, is on track to become the world's second-largest drug market by 2015.

As reported in SupplyChainBrain, "the most predominant change in customer needs will come from a sheer increase in the volume of drugs and medical supplies demanded. In order to cement a piece of the expanding market, distributors will be tasked with widening their networks and investing in the infrastructure and technology to support them."

Increased Number of Product Lines

According to the 2014 Cardinal Health annual report, the company manufactures nearly two billion consumer healthcare, home medical equipment and over-the-counter products each year. The company also launched 500 new SKUs during that single year.

This in keeping with overall industry trends, which has seen explosive growth in the number of SKUs. Increasingly complex products and diverse consumer preferences have resulted in the typical plant now handling double the amount of SKUs it processed ten years ago. For example, SupplyChainBrain notes the use of injectable cancer treatments has increased by 20 percent in recent years. By 2016, bioengineered vaccines and biologics are expected to account for 23 percent of the global market, up from 17 percent during 2009.

There has also been a dramatic increase in the number of medicines requiring refrigeration and associated special handling. The 2014 Biopharma Cold Chain Sourcebook, which tracks data and trends in the pharmaceutical industry, estimates that spending on "cold chain" logistics – the packaging and distribution necessary to transport biologically-originating drugs – will increase to $9.3 billion by 2017, a 20 percent increase over 2013 levels. Proper temperature control is also regarded as a security issue, since a slight variation in temperature could be enough to spoil a pharmaceutical, rendering it ineffective, or even harmful.

The results have been increasingly complex production and distribution processes, that have added strain to the supply chain. "Complexity is painful for supply chain managers," wrote McKinsey researchers in a PharmaManufacturing.com article, "in part because it makes volatility more expensive to handle: Inventories must double to maintain the same service level across twice the number of SKUs, for instance."

A worst-case result, is a supply chain disruption, or product shortage. SupplyChainBrain reports that during 2012 alone, thee were more than 100 reported disruptions in the supply of crucial medications. This in turn has increased pressure on

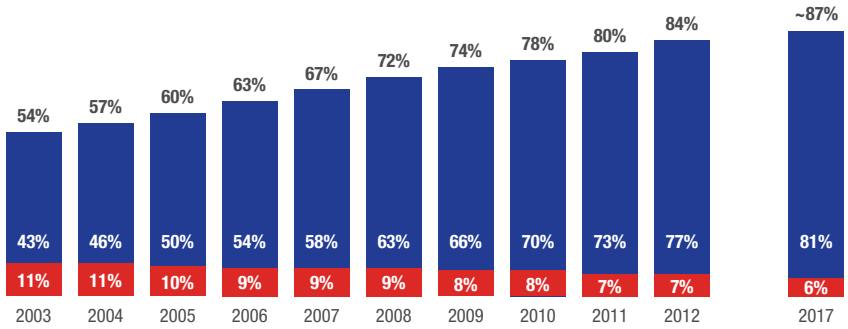
manufacturers to increase production, with suppliers squeezed to offer more efficient distribution solutions.

Surge in Generics

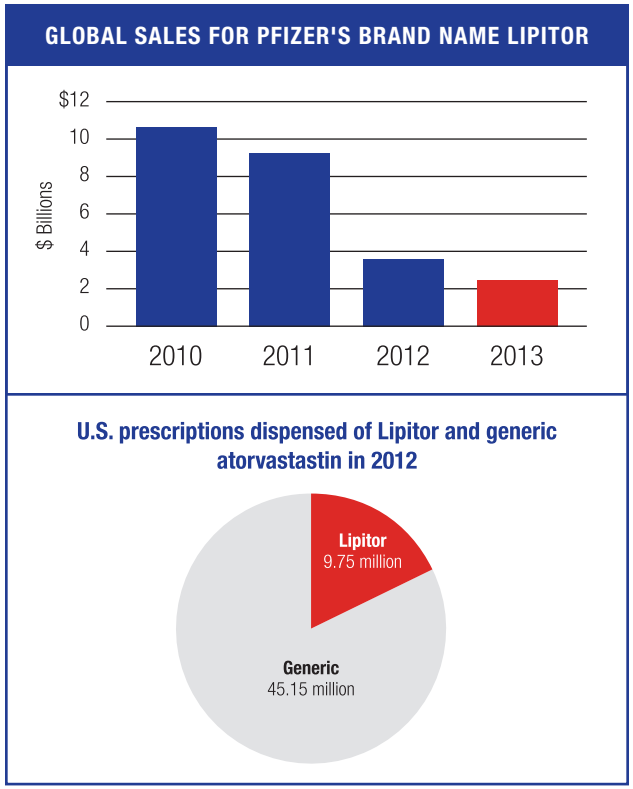
Traditional pharmaceutical supply chains have been significantly impacted by the explosion of generic drugs on the global marketplace. During 2012, generic drugs accounted for roughly 84 percent of the world's prescription drugs. This has been primarily the result of a "Patent Cliff" that has taken hold in the pharmaceutical world, marked by the expiration of patents for some of the world's best selling, and most profitable medicines. The trend is expected to continue through 2018. In general, generic drugs cost 75 percent less than their branded-counterparts, which have left drug companies scrambling to find ways to replace, or offset the loss in revenue. The supply chain has been an obvious place for many companies to look, with added pressure for managers to find efficiencies and cut costs.

To fully understand the impact generics have had, consider the case of cholesterol-fighting Lipitor, manufactured by Pfizer. Lipitor generated billions of dollars of revenue for Pfizer, topping out at nearly $13 billion annually, until its patent expired during 2011. Soon after, the market was flooded with generic versions of the drug, and Lipitor sales plummeted. In an effort to breathe life back into the brand, Pfizer recently petitioned the FDA to try and gain approval for an over-the-counter version of the drug.

SURGE IN GENERIC DRUGS 2003-2017



Source: IMS Health National Prescription Audit, December 2012



Source: As depicted in SupplyChainBrain, Sept/Oct 2014

For generic manufacturers, speed to market is essential. Once a brand name drug is no longer patent-protected, there is quite literally a race among generic manufacturers to be first to bring a generic alternative to market. "Generics have a very short window of profitability," explained one 3PL manager who specializes in health products logistics. "Once the drug goes off patent, the first one to market wins. Manufacturers have a 30- to 60-day window to make huge profits, and then it starts to level out."

But speed and efficiency are not the only hurdles a generic manufacturer must clear. The drug must meet all FDA guidelines before it can enter the market, and in some instances, the FDA may impose specific labeling requirements.

Supply Chain Security

With so much at stake, it is not surprising that supply chain security is a major concern for manufacturers of healthcare products. While the U.S. Food and Drug Administration has regulatory control over all drugs and medicines sold in the U.S., and Health Canada is charged with oversight of our largest trading partner's pharmaceutical products, non-regulatory threats including disruptions, counterfeiting and theft are constant supply chain challenges.

Although medicines and medical devices are among the most regulated products in the world, they are top targets for counterfeiters. This is because fake products can be produced at a relatively low cost, and because lax standards in many developing countries allow relatively easy entry to many consumer markets. Counterfeit drugs are a $35-$40 billion per year industry, and can be found in markets worldwide. Counterfeits pose a tremendous risk to public safety, and

eliminating counterfeiting risk from the supply chain is a top priority for manufacturers, regulators and law enforcement officials worldwide.

In the United States and Canada, joint government-business programs have been established as a way to certify each manufacturer's supply chain. Through the U.S. Customs-Trade Partnership Against Terrorism (C-TPAT) program, and Canada's Partners in Protection (PIP), businesses agree to certify the security of their supply chains – and their vendors' supply chains – in exchange for preferential border clearance treatment including expedited clearance.

Technology has helped make tremendous inroads with supply chain security. State of the art technology systems can ensure 24/7 product visibility and trace/tracking capability. Where possible, manufacturers are using RFID technology, although placement of RFID tags has been found to affect certain types of medicines.

Product Returns

Unlike regular consumer returns that can often be reintroduced into the market via an online auction site or retail outlet, pharmaceutical returns must follow a very careful reverse logistics course, usually ending in product destruction.

Pharmaceutical products have been increasingly subject to regulatory recalls. During 2013 the FDA issued a record 1,225 product recalls, and is on track to surpass that number during 2014.

FDA PRODUCT RECALLS 2004-2014*

YEAR	TOTAL RECALLS
2014* * Year as of August 11 2014	836
2013	1,225
2012	499
2011	444
2010	246
2009	164
2008	203
2007	126
2006	116
2005	253
2004	166

Source: Regulatory Affairs Professional Society, August 2014.

While there is no definitive reason for the increased number of recalls, speculation is that the Agency began to take a more assertive stance in 2012, following a deadly outbreak of fungal meningitis. Other reasons may include lapses in current Good Manufacturing Practices (cGMP) which may have caught the eye of FDA regulators.

Whatever the reason, manufacturers need to plan for the possibility of a recall at any time, for any reason. The FDA has very detailed and specific protocols in place should a product be recalled. A manufacturer must submit detailed information about the product's supply chain, and must also include detailed information about how the recalled product will be removed from the market, and how consumers can protect themselves.

Beyond that, businesses should have in place a detailed "recall manual," which details the roles and responsibilities of every functional area during a recall. Integral of course, will be the actual processes of (a) stopping any additional shipments from going out; (b) implementing a reverse supply chain in order to collect product that has already been shipped and to trace products as far down the chain as possible; (c) store or dispose of affected products; and (d) provide remedy to affected businesses and consumers.

Recalls are not the only reason for pharmaceutical returns. Every year as much as $4.2 billion in expired product is returned to pharmaceutical manufacturers. A white paper from the Healthcare Distribution Management Association cites five top reasons why product remains in inventory beyond its expiration date:

1. Patients decide to obtain medicine from a different source (pharmacy, clinic, mail order)
2. Patients shorten or end their prescribed drug regimen
3. Patients move to a generic equivalent or a different course of treatment
4. Retailers compete aggressively for consumers' business
5. Negative information materializes about a drug product

Whatever the reason, a manufacturer needs to have in place a process for retrieving the expired product as quickly as possible and ensuring its proper disposal. This can be accomplished by working with your logistics partner, who presumably has the necessary experience, to develop a strategy to collect the expired product, issue proper credits, store the products and then transport to their ultimate destination, presumably for destruction.

Another critical factor though, is taking steps to prevent products from becoming expired before they are sold. A key recommendation would be to add visibility into the supply chain so that managers can track pharmacies with slower-moving medicines, and move those products to locations where they are more likely to sell. Visibility would also ensure that pharmacies and retailers regularly rotate stock, and that production levels are aligned to reflect true demand.

Regulatory Issues

Healthcare product manufacturers also face stringent – and growing – regulatory and legislative mandates designed to ensure the safety and effectiveness of products intended for public consumption and use. While U.S. and Canadian manufacturers and retailers have long understood the need for FDA and Health Canada compliance, the globalization of the supply chain has in many ways been regulatory game changer.

Today nearly 40 percent of all drugs dispensed in the United States are manufactured outside the country, and nearly 80 percent of the ingredients are manufactured abroad. This means a product intended for use in the U.S. or Canada must travel long distances and cross several borders before arriving in its intended location. And it must comply with myriad local regulations along the way.

One pharmaceutical logistics expert says "Pharmaceutical industry service providers need to be aware of about 70 different sets of regulations." Clearly this is not sustainable, and initial talks have begun to establish some degree of uniformity for international collaboration. The U.S. Pharmacopeial Convention (USP), is one organization that works to set standards that are recognized internationally. USP's drug standards are enforceable in the U.S. by the FDA, and are also used in more than 140 countries, including Canada. The International Conference on Hamonisation (ICH) is another international organization working to streamline regulatory mandates.

Specific to U.S./Canada cross border trade, efforts are underway to facilitate the clearance process for pharmaceuticals, over-the-counter medicines and medical devices. In 2011 President Barack Obama and Canadian Prime Minister Stephen Harper announced an agreement called "Beyond the Border" as a way to improve border security and promote economic opportunities between the two countries. Integral to the Beyond the Border initiative, is the Canada-U.S. Regulatory Cooperation Council (RCC), which outlines new approaches to regulatory cooperation for several key industries, including healthcare products.

The agreement, which is still in the development stages calls for development of a common electronic filing system for pharmaceutical and biological products, and cross border recognition of each country's supply chain security programs, namely CBP's Customs-Trade Partnership Against Terrorism (C-TPAT) and CBSA's Partners in Protection (PIP).

While the U.S. and Canada look to a future that includes a shared regulatory environment and common labeling and packaging mandates, the reality is each country will continue to maintain separate regulations and mandates with regard to transporting healthcare products across international borders.

FOUR OF THE LEADING PHARMACEUTICAL COMPANIES IN CANADA ARE U.S. -BASED			
RANK	LEADING COMPANIES	TOTAL SALES ($ BILLIONS)	MARKET SHARE (%)
1	**Johnson & Johnson (U.S.)**	**1.89**	**8.6**
2	**Pfizer (U.S.)**	**1.60**	**7.2**
3	Apotex (Canada)	1.27	5.7
4	AstraZeneca (U.K./Switzerland)	1.22	5.5
5	**Merck (U.S.)**	**1.11**	**5.0**
6	Teva (Israel)	1.03	4.7
7	Novartis (Switzerland)	0.99	4.5
8	**Abbott (U.S.)**	**0.95**	**4.3**
9	GlaxoSmithKline (U.K.)	0.95	4.3
10	Pharmascience (Canada)	0.77	3.5

Source: http://www.ic.gc.ca/eic/site/lsg-pdsv.nsf/eng/h_hn01703.html

Facilitating a positive trade environment is a priority of both governments. The U.S. is the top destination for Canadian pharmaceutical exports, and relies on the U.S. for more than 34 percent of its imports. Based on 2012 data, four of the top ten pharmaceutical companies in Canada, were U.S.-based.

Exporting Health Products from the United States

The U.S. Food and Drug Administration is the U.S. agency with direct control over healthcare products entering and leaving the country. FDA compliance is in addition to Customs Border Protection (CBP) security and customs requirements, and other agencies that may have jurisdiction in certain circumstances.

FDA/EXPORT OF MEDICAL DEVICES

With regard to medical devices, any medical device that is legally in the U.S. may be exported anywhere in the world without prior FDA notification or approval. Devices that have not been approved or cleared in the U.S. must follow specific export provisions of the Food, Drug and Cosmetics Act (FD&C).

In general, non-approved devices (which are considered 'for export only') may be exported and without FDA approval if they meet the following conditions:

- If they are in accordance with the specifications of the foreign purchaser;
- If they are not in conflict with the laws of the country to which they are intended for export;
- If they are labeled on the outside of the shipping package that they are intended for export; and
- If they are not sold or distributed in the United States.

According to the FDA, depending on which section of the FD&C Act a specific medical device falls under, it may be necessary to obtain an export permit letter, or an export certificate to present to the country of importation. Through the FDA export certificate, the agency affirms that a manufacturer has met specific standards for "good marketing practices," and that the products in question "either meet the applicable requirements of the Act and may be legally marketed in the United States, or may be legally exported under the Act, although they may not be legally marketed in the United States." Different types of export certificates are available, depending on the contents and characteristics of the product to be exported.

FDA/EXPORT OF PHARMACEUTICAL PRODUCTS

U.S. pharmaceutical manufacturers wishing to export must comply with several regulations, similar to those that must be followed by medical device manufacturers. In addition to an export certificate, the Center for Drug Evaluation and Research (CDER), requires specific coding as follows:

- For drug products that are legally marketable in the U.S., a RED ribbon will be affixed to its "Certificate of Pharmaceutical Product" export certificate.
- Products not authorized for sale in the U.S. and manufactured for export only that are legally eligible for exportation must have a BLUE ribbon affixed to the mandatory Certificate for Export of an Unapproved Product.
- Products manufactured outside of the United States must have a YELLOW ribbon affixed to the mandatory "Certificate to Foreign Government."

The FDA also establishes numerous manufacturing, processing, packaging and distribution requirements for drugs, biological products and medical devices scheduled for exportation. The FDA regulates the shipment of all temperature sensitive products, for example.

In general, all export requirements are established by the FDA Export Reform and Enhancement Act of 1996, and its subsequent amendments. Unless a manufacturer has the resources and expertise to understand the minutiae of this detailed statute, it is highly recommended that services be enlisted of a customs broker or qualified logistics, to ensure full compliance.

For example, consider labeling requirements. The FDA requires that if a drug approved for sale in the U.S. is exported to a country that has different labeling requirements or conditions for use, the product may be labeled in accordance with the foreign country's requirements, so long as the label also states that those conditions are not approved in the United States.

Another key consideration is compliance with the "Drug Supply Chain Security Act of 2013," which will be phased in over the next ten years. Among other things, the legislation includes "track and trace" provisions that will require:

- Product Identification. Manufacturers will need to put a unique product identifier on certain prescription drug packages. This could include a bar code that can be read electronically.
- Product tracing. Manufacturers, wholesale drug distributors, dispensers and others in the drug supply chain will be required to provide information about a drug, including who specifically handled it, each time it passes hands in the U.S. market.

The Act also calls for a national electronic system to identify and trace certain drugs as they move through the supply chain. As these provisions are implemented over the next ten years, it is probable that manufacturers will need to adapt and change current practices, and implement new compliance systems. This again highlights the critical importance of having a customs broker to interpret the new regulations and ensure compliance.

RECORD KEEPING

Another key requirement of the FDA is that detailed records be maintained for all drugs and devices exported from the United States. The precise requirements are outlined in the Export Reform Act of 1996. Following is a listing of some – not all – of the Act's documentation requirements:

- The product's trade name;
- If the product is a drug or biological product, a description of its strength and dosage form and the product's lot or control number or, if the product is a device, the product's model number;
- The importer's name and address; and
- The date on which the product was exported and the quantity of product exported.

The FDA requires that these records be kept at the site from which the product was exported and for a certain period of time, depending on the product.

Importing Healthcare Products to Canada

Health Canada is the Canadian government agency with primary responsibility for healthcare products arriving in Canada from other countries. Health Canada regulations are in addition to requirements mandated by the Canada Border Services Agency (CBSA), and other agencies with jurisdiction over the import process.

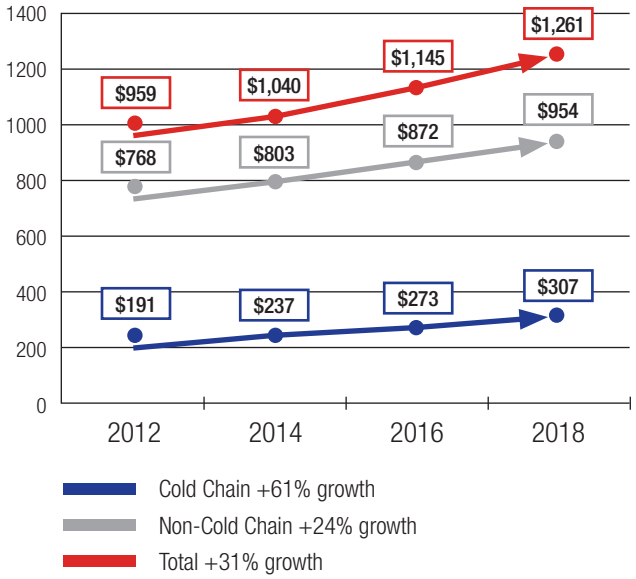
U.S. manufacturers are often quick to learn that Health Canada's import requirements are exacting, and can vary from FDA requirements for the same product.

Of special interest to supply chain managers and transportation provider is Health Canada's "Guidelines for Temperature Control of Drug Products during Storage and Transportation – (GUI-0069." This document, also referred to as "Guide 69," establishes procedures for all cold chain distribution, warehousing and transportation practices, and emphasizes the need for training in warehousing and storage. According to the document, drugs should be stored "according to the label requirements" at a minimum.

"Drug products must be transported in a manner that ensure the products will be maintained within an acceptable temperature range as defined in the approved labeling and supported by stability data," the Guide further reads.

INCREASED VALUE OF PRODUCTS REQUIRING COLD CHAIN PROCESSING

Global Biopharma Sales ($billions) trend 2012-2018



Source: http://pharmaceuticalcommerce.com/sourcebook_intro

Speaking at the 2014 Cold Chain and Temperature Summit Canada, Health Canada compliance specialist Sarah Skuce noted that Guide 69 is "inclusive of all drug products, all

pharmaceuticals, veterinary and human. All regulated parties are covered in the guide. Transport providers are not covered but are expected to follow the guidelines."

Skuce also noted the increased vigilance by customs officers to ensure that all protocols have been followed. "There must always be quality control sign off for actions taken after an excursion," she said. "The pharma industry should be aware that inspectors will follow products from the receiving end through the entire process."

In addition to cold chain pharmaceuticals, manufacturers need to be aware of Health Canada regulations for all drugs and medical devices before they reach the U.S./Canadian border.

HEALTH CANADA/MEDICAL DEVICES

Canada enforces a four-tier classification system for medical devices, based on a product's affect on the human body. Class I devices represent the lowest risk (e.g. a thermometer or bandage), and Class IV devices pose the highest risk (e.g. a pacemaker). Prior to selling a device in Canada, a Medical Device License is required for manufacturers of Class II, III and IV devices. Manufacturers of Class I devices are monitored through Establishment Licenses, which requires the manufacturer to list the establishments that will be selling its devices.

Following is a list of Health Canada requirements for commercial importation of each category of medical device:

HEALTH CANADA REQUIREMENTS FOR COMMERCIAL IMPORTATION OF MEDICAL DEVICES

COMMERCIAL IMPORTATIONS	HEALTH CANADA REQUIREMENTS
Class I devices. (examples: bandage, wheelchairs, bed scales, hospital beds/stretchers and crutches)	• Device License not required. • Importer must have an Establishment License (EL); see list below table for those entities that are exempt from needing an EL(*).
Class II, III and IV devices. (examples: gauze pads, electronic stethoscopes, electrodes, hearing aids, medical examination gloves, scalpels, electrocardiographs, blood pressure cuffs, latex condoms, pregnancy tests, defibrillators, infusion pumps, bacteria and drug test kits, hyperbaric oxygen therapy chambers, implants, insulin pumps and cardiac pacemakers, glucose testing systems, embolectomy and occlusion catheters, balloon thermodilution catheters, blood catheters, central venous catheter kits, aneurysm clips, excimer laser and intraocular lens)	• Device License not required. • Importer must have an Establishment License (EL); see list below table for those entities that are exempt from needing an EL(*).
Investigational testing devices to be used on human subjects	• Require identification as "Investigational Device" on the label of the device. • Letter of Authorization (LOA) issued by the Medical Device Bureau (MDB) must accompany Class II, III and IV devices under Investigational Testing status.
Special Access and Custom-made devices.	• Label must specify that the device is custom-made or for Special Access. • Letter of Authorization (LOA) issued by the Medical Device Bureau (MDB) must accompany all classes of Special Access devices; and class III and IV custom-made devices.

(*)The following entities are exempt from the requirement of having an Establishment License (EL) to import medical devices:

1. A Retailer;
2. A Healthcare Facility;
3. Manufacturers of Class I devices if the manufacturer imports or distributes through a person who holds an Establishment License;
4. A person who only imports a medical device for their own personal use;
5. Establishments only importing or selling veterinary products;
6. Dispensers; and
7. Establishments that only import or sell custom-made devices, medical devices for Special Access, or devices for Investigational Testing involving human subjects.

HEALTH CANADA/PHARMACEUTICALS

Drugs for human consumption (i.e. not for veterinary purposes) are categorized by Canada's Food and Drug Act into several different categories:

- Schedule C: Includes all radiopharmaceuticals excluding radionuclies;
- Schedule D: Includes drugs derived from human, animal or microbial sources such as insulin and blood-based products;
- Schedule F: Prescription Drugs
- Over the Counter Drugs
- Products Imported under the Special Access Program
- Human Drugs imported for use in a clinical trial

Following is a list of commercial importation requirements for each category. Please note though, that some drugs may also be subject to restrictions issued by other legislative mandates, such as the Controlled Drugs and Substances Act. According to Health Canada, "where two different restrictions/requirements exist, such as the quantity allowed for importation, the most restrictive or prescriptive will take precedence."

In addition to compliance with the above licensing and quality mandates, U.S. businesses must also comply with Health Canada regulations for labeling, marketing restrictions and compliance with all "good market practices" as outlined in the Food and Drugs Act.

HEALTH CANADA REQUIREMENTS FOR COMMERCIAL IMPORTATION OF PHARMACEUTICALS

COMMERCIAL IMPORTATIONS	HEALTH CANADA REQUIREMENTS
Schedule C (Radiopharmaceuticals excluding radionuclides)	• No Drug Identification Number (DIN) required. • Importer must hold an Establishment License (EL). • The foreign manufacturing site must be listed on the Importer's EL.
Schedule D drugs (Drugs derived from Human, Animal or microbial sources, such as insulin and blood based products)	• A Drug Identification Number (DIN) for each product. • Importer must hold an Establishment License (EL). • The foreign manufacturing site must be listed on the Importer's EL.
Prescription Drugs (Schedule F)	• A Drug Identification Number (DIN) for each product. • Importer must hold an Establishment License (EL) and also must be a practitioner, a drug manufacturer, a wholesale druggist or a registered pharmacist. • The foreign manufacturing site must be listed on the Importer's EL.
Over the counter drugs (OTC)	• A Drug Identification Number (DIN) for each product. • Importer must hold an Establishment License (EL). • The foreign manufacturing site must be listed on the Importer's EL.
Products imported under the Special Access Programme (SAP)	• A Letter of Authorization (LOA) issued by the Special Access Programme (SAP) of Health Canada authorizing the sale/use of a pharmaceutical product for each instance. A copy of this authorization must be provided at the port of entry.
Human Drugs imported for use in a clinical trial (Other than phase IV)	• A No Objection Letter (NOL) issued by the Therapeutic Products Directorate (TPD) or the Biologics and Genetic Therapies Directorate (BGTD) of Health Canada authorizing the use of the drug in a clinical trial for each drug/trial. A copy of this authorization must be provided at the port of entry.

These restrictions are very detailed and voluminous. With regard to labeling, products sold in Canada must comply with numerous regulations which may include:

- Directions for use must be printed both in French and English;
- The name and address of the manufacturer/sponsor and of the distributor must be printed on the label, if the manufacturer/sponsor is not Canadian; and
- The notation "sterile (stérile)" must appear on the label.

RECORD KEEPING

U.S. manufacturers that export healthcare products to Canada are required to maintain all associated records for "at least seven years from the day on which they were established." This seven-year requirement was announced in May 2014, as a way to align Canadian requirements with international "good marketing practices-based" retention requirements, which have been adopted in the United States and Europe.

In addition, cold chain logistics providers are required to maintain detailed documentation with regard to chain of custody. And, according to Health Canada compliance specialist Sarah Skuce, the Agency has stepped up its oversight. "If you do not record it or document it," she said, "then it never happened."

CBSA – ADDITIONAL IMPORT REQUIREMENTS

The above discussion on U.S. FDA and Health Canada requirements for cross border treatment of healthcare products is in addition to customs and security mandates enforced by U.S. Customs Border Protection and the Canada Border Services Agency.

Following is an abbreviated overview of regulations a U.S. business exporting to Canada may face:

- **Business Number.** Any business importing or exporting goods to Canada must register with the Canada Revenue Agency and be issued a business number that must be used on all paperwork, which is used to track all customs-related documentation and payments.
- **Cargo control document (CCD).** Canada Border Services Agency (CBSA) requires that a cargo control document accompany each shipment. The CCD is also referred to as a manifest, and includes an itemized list of the contents included in a shipment.
- **Commercial Invoice or Canada Customs Invoice.** A commercial invoice is the primary document a buyer/importer uses to pay a vendor/exporter, and generally includes information including: description of the goods, direct shipment date, tariff treatment, country of origin, tariff classification, value for duty, appropriate duty or tax rates and calculation of duties owed.

- **Canada Customs Coding Form - B3:** CBSA requires Form B3 as a way to account for goods, regardless of their value, for commercial use in Canada. This document captures a wide range of information about each shipment including country of origin, tariff treatment, mode of transport and tax liabilities.
- **NAFTA Certificate of Origin.** Shipments eligible for preferential treatment as outlined by the North American Free Trade Agreement must be accompanied by a Certificate of Origin. This document includes detailed information about the contents of a shipment, including the origination of each component part. The Certificate or Origin is not required for non-NAFTA shipments, or for shipments valued at less than US$1,000.
- **Import Permits.** CBSA assists other government departments (OGDs) in administering entry requirements for products that fall within their areas of control. For pharmaceuticals and medical devices, this would generally trigger Health Canada regulations. The U.S. Commercial Service advises that securing the necessary permits can be time consuming, and that attending to potential OGD requirements should be "one of the first steps taken" in initiating the export process.

DUTIES AND FEES.

Critically important to doing business in Canada is an understanding of that country's unique sales tax code. Sales taxes are collected at the federal and provincial levels of government, and a business must be careful to comply with all applicable levies. Please note that sales taxes are different from import duties.

- A federal Goods and Services Tax (GST) of five percent of value is assessed on just about all goods entering the country.
- Provincial sales taxes are levied at the province level, and are collected locally.
- The provinces of Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador, and Ontario have opted to "harmonize" their provincial sales tax with the general sales tax. This combined rate is called the "harmonized tax," and represents the sum of the 5 percent federal GST plus the appropriate provincial tax.

Depending on the items being shipped, goods may also be subject to excise taxes and other fees. Another important thing to understand about the Canadian tax code – it is subject to change, and without much notice. Businesses are responsible for keeping abreast of all tax policy changes, and for ensuring that correct taxes are collected and paid.

Supply Chain Solutions

While few supply chains can be considered "easy" or "routine," it's safe to say that moving healthcare products through a manufacturing and distribution process requires a high degree of competence, skill and commitment. Health products supply chains are unforgiving, when even the slightest delay can result in a devastating drug supply shortage, or a manufacturing mistake can literally end up placing people's lives in danger, or force a business to lose millions of dollars in a product recall.

Fortunately, innovative thinking and technological advancements have made tremendous inroads in recent years. Today, a well-managed supply chain includes a high degree of visibility, shortened transit times and flawless compliance processes. Following is a brief overview of some suggestions that may help your business improve its health products supply chain efficiency.

Choosing the Right Logistics Provider

This cannot be overstated. Choosing the right partner to oversee implementation of its supply chain is one of the top decisions a manager will make. A poor choice here could reverberate throughout the entire organization, and damage not only your company's reputation, but endanger the health and safety of your customers.

But with so many logistics providers to choose from, how do you know which is the right choice?

When it comes to finding a logistics partner to handle the unique needs of a pharmaceutical and/or medical device manufacturer and the nuances of shipping to Canada, there is no match for experience. Many providers claim to offer these specialized services, but as many businesses have learned the hard way, saying you can transport a shipment of drugs to Canada, and actually having done it, are often two different things. With regard to finding the best Canadian provider, here are a few considerations:

- **Experience.** How long has the provider been operating in the Canadian market, and what types of solutions do they offer? Is the provider willing to share a list of customers? If a firm is reluctant to ask their current customers to discuss their experiences, it might be because the feedback will be less than stellar.
- **Training.** When it comes to building a pharmaceutical or medical devices supply chain, every employee must be aware of the nature of the products, the highly regulated environment, and the need for special care and attention to detail. As such, a reputable logistics provider will ensure that only the most capable employees are allowed to work with these products, and will ensure provide training on proper handling and compliance processes.

- **Customer Service.** Good customer service will be vitally important, especially in the unlikely event there is an unforeseen disruption. An experienced logistics partner will designate key personnel to service your account, who will have total insight and understanding of your business objectives. That way, your customer service agent can suggest alternate solutions should something go awry, and very often can resolve a problem before you even know about it!
- **Specialized Equipment.** If your shipments require refrigerated trucks, or expedited delivery, or a high degree of security, it's essential that the logistics partner you select have the assets necessary to complete the job. You don't want to find out too late that your logistics partner has no Canadian distribution network, and plans to off load your precious shipments to an unknown third party provider.
- **Language Requirements.** Don't forget that Canada is officially a bilingual country, with more than one-third of the population listing French as their preferred language.
- **Flexibility.** Can the provider offer the services that fit your specific needs, or will you be required to adjust your needs to fit what the provider can offer?
- **Scope of Service.** Can the provider offer comprehensive solutions for all logistics needs, or are businesses required to settle for a rigid "one size fits all" service option? Will you be forced to pay for levels of service you do not need – overnight delivery, for example, when 2-day would suffice?
- **Customs Expertise.** As the preceding discussion makes clear, customs expertise is vitally important for the cross border movement of pharmaceuticals and medical devices. Ask a lot of questions. What type of expertise does the firm offer for managing the customs process? Is the process managed internally or outsourced to a third party customs broker? Is the logistics provider a participant in any U.S./Canadian trusted trade programs? What capability does the provider offer to assure that shipments clear the border hassle free, and as cost-effectively as possible?

As an example of the type of service you should expect from your logistics provider, consider the following: Health Canada places responsibility for compliance with all regulatory and legislative requirements with the importer. Under "normal" circumstances, that would mean a Canadian business purchasing a medical device or pharmaceutical from a U.S. business would need to become involved in the customs process. Fortunately, the Canadian government offers a "Non-Resident Importer" program, which allows the U.S. manufacturer to act as the importer of record.

Among the many benefits of being an importer of record, is the ability to intervene in all customs transactions, thereby relieving the Canadian business of the responsibility. Non-resident importers are also able to charge Canadian sales tax at the time of purchase, and provide their Canadian customers with a comprehensive bill up front, which means customers will not be assessed with unexpected additional invoices at time of delivery.

As helpful as the Non-Resident Importer program is though, many U.S. businesses do not take advantage, mainly because they do not know it exists. A good logistics provider will not only know about the program, but will help a business navigate the application process. The same is true of other border clearance facilitation programs including CBP's Customs-Trade Partnership Against Terrorism, which gives preferential treatment to approved U.S. businesses that certify the security of their supply chains.

A business that takes the time to research its options will realize that when it comes to managing cross border shipments, not many logistics providers offer the right combination of Canadian customs expertise and health products logistics skill. But, do not sacrifice! Finding the right logistics partner is a critical part of improving supply chain efficiency, and can be integral to success in the Canadian market.

Improving Processing and Distribution Efficiency

Processing, warehousing and distribution of healthcare products naturally trigger very specific – and often mandated – requirements that demand specialization, a highly-trained workforce and a technology component that links all parts and ensures efficiency. The good news though, is that tremendous innovations are now available to ensure higher degrees of efficiency and flawless execution.

Warehousing. Any warehouse that services pharmaceuticals and/or medical devices needs the capabilities required for managing temperature-dependent, time-critical, highly regulated products. At the same time, warehouses need to be located in geographically advantageous locations that fit with the company's overall logistics needs.

Security: State of the art warehouses will include vaults with motion detector alarms, or electronic security systems that require employees to swipe an identification card to gain access to areas where narcotics or very expensive drugs or devices are stored. In addition, in some cases, a warehouse operator will remove samples of a particular drug, and have it tested to make certain no tampering has occurred. Only after receiving assurances from a laboratory will the drug then be removed from the warehouse.

Temperature Control. Warehouses – and trucks – are now equipped with technology-controlled refrigeration systems that continually monitor product temperature, and will trigger an alarm should any fluctuation in climate occur. In addition, warehouses can provide temperature-controlled docks, so that products enter and leave a warehouse without ever having to be in a non-controlled environment.

Packaging. Traditional Styrofoam coolers and gel packs are slowly going the way of the dinosaur as packaging innovations have become more efficient. New materials and designs have led to the introduction of several new options of reusable, strong, high-performing options.

Find your Best Transportation Solution

Aside from these industry-specific requirements, it is essential to ensure that products are traveling via the most appropriate transportation solution. And this again is where an experienced logistics provider will choose from its range of options to offer a customized solution that best meets a business' precise needs.

Expedited Services. Since few shipments require the care and attention – or regulatory control – inherent to pharmaceuticals, it's not surprising then that expedited service is an increasingly preferred logistics option. But unlike many industries that rely on expedited service for speed, health products manufacturers turn to it for security, product integrity and regulatory compliance. According to the Journal of Commerce (JOC), the FDA considers "transportation" to be part of the manufacturing process, with manufacturers liable for compliance steps taken by their transportation providers. Expedited service allows manufacturers the added comfort of knowing their products are being handled via premium service.

Other businesses gravitate to expedited service because of its high degree of customer service. Once experienced expediter told JOC that security is his pharmaceutical customers' top concern. "A lot of customers will require team drivers on a load that will only go 250 to 300 miles," he said. "That's not about hours of service or expediting a shipment, it's about redundancy and mitigating risk by layering on security."

Temperature control is another consideration. Manufacturers are expected to spend $8.36 billion during 2014 on temperature-controlled shipping, an increase from the $7.5 billion spent during 2013. Cold-chain costs include shipping and storage costs along with customized packaging including insulted and refrigerated containers in which products are transported. According to the Biopharma Cold Chain Sourcebook, published by Pharmaceutical Commerce magazine, cold chain spending accounts for a small but growing part of the overall $55.3 billion global biopharma logistics market.

A key challenge for pharmaceutical businesses, is the extremely restrictive environment in which they operate, due to regulatory compliance mandates. Cost saving options available to other industries are often off limits. A particular issue is finding better last-mile delivery solutions for temperature controlled products, and ensuring that a logistics provider has adequate monitoring and tracking devices to detect any mid-shipment changes in temperature, light, vibration, humidity and, in the case of air shipments, elevation.

Consolidation is King. Shipments that may not need the "rolls royce touch" inherent to expedited service can benefit from a more efficient LTL experience, namely though consolidation. Combining smaller shipments into one larger unit can be a tremendous source of savings. This can be accomplished in a number of ways: Placing multiple orders in the same carton, banding multiple cartons together, palletizing shipments, or using a full truck. By some estimates, consolidation can reduce freight costs by as much as 10 percent. But again, great care must be taken to ensure regulatory compliance, ensure that only like-drugs are consolidated, and to minimize risk of damage or spoilage.

Route Optimization. Among the many positive contributions technology has made to the freight/logistics industry, the concept of route optimization has been among the most beneficial. Route optimization software helps companies better manage their distribution networks through the use of advanced algorithms. The process calculates the most efficient service option, maps out direct routes, and matches available trucks and drivers to make the delivery. In doing so, delivery routes become much more streamlined, meaning reduced mileage and lower fuel costs.

Conclusion

A 2014 survey of healthcare executives found that regulatory compliance and increasing regulations are the biggest influencers of business and supply chain decisions. But rather than throw their hands up in frustration, the survey also found that most executives are determined to improve efficiency in spite of the omnipresent regulatory cloud. Sixty percent said they are working with an external logistics provider, for example, to find efficiencies and improve competitiveness, while others cited increased collaboration and partnerships.

It certainly is a time of transition in the pharmaceutical and medical devices industries. In addition to the regulatory burden, demands of the global marketplace, new treatments and product lines, along with a proliferation of generic drugs, have all combined to create a new "normal" for manufacturers.

As business managers plan their way forward, they quickly learn that a qualified and trusted logistics provider is their essential partner. With so much at stake, the right logistics partner can truly offer supply chain efficiency and much-needed peace of mind.

Purolator. We deliver Canada.

Purolator is the best-kept secret among leading U.S. companies who need reliable, efficient, and cost-effective shipping to Canada. We deliver unsurpassed Canadian expertise because of our Canadian roots, U.S. reach, and exclusive focus on cross-border shipping.

Every day, Purolator delivers more than 1,000,000 packages. With the largest dedicated air fleet and ground network, including hybrid vehicles, and more guaranteed delivery points in Canada than anyone else, we are part of the fifth largest postal organization in the world.

But size alone doesn't make Purolator different. We also understand that the needs of no two customers are the same. We can design the right mix of proprietary services that will make your shipments to Canada hassle free at every point in the supply chain.

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References

"30+ RCC Shareholders Emphasize Support for Joint Forward Plan, Press for 'Additional Specific and More Concrete Details,'" Beyond the Border Observer, Wilton Center, October 15, 2014.

Biggar, Kim, "Accuristix: Thriving in the Highly-Regulated Health-Care Sector," 3PL Americas, International Warehouse Logistics Association, December 2012.

"Business Transformation and the Regulatory Environment," KPMG Transformation Survey, 2014.

"Canada-United States Regulatory Cooperation Joint Forward Plan August 2014," Canada's Economic Action Plan, August 2014.

Douglas, Merrill, "Navigating Pharma Logistics," Inbound Logistics, August 2012.

"Drug Supply Chain Security Act," U.S. Food and Drug Administration website, accessed October 23, 2014.

"Essential to Care," Cardinal Health, Inc. annual report, 2014.

"Exporting Medical Devices," U.S. Food and Drug Administration website, accessed October 23, 2014.

"Exporting Unapproved Devices," U.S. Food and Drug Administration website, accessed October 23, 2014.

"Exports Under the FDA Export Reform and Enhancement Act of 1996," U.S. Food and Drug Administration website, accessed October 23, 2014.

"FDA Export Certificates," U.S. Food and Drug Administration website, accessed October 23, 2014.

Gaffney, Alexander, "Number of Drug Recalls Surges at FDA, Led by Mid-Level Concerns," Regulatory Affairs Professional Society, August 2014.

"Global pharma industry will spend $8.36 billion on cold-chain logistics in 2014," Pharamaceuticalcommerce.com, March 31, 2014.

Gordon, Benjamin and Milstein, Daniel, "Industry-Altering Changes Occur in Life Sciences Supply Chain," Supply Chain Brain, September-October 2014.

"Guidance Document on the Import Requirements for Health Products under the Food and Drugs Act and its Regulations," Health Canada website, accessed October 23, 2014.

"Guidance Document Labeling of Pharmaceutical Drugs for Human Use," Health Canada website, accessed October 24, 2014.

"Guidelines for Temperature Control of Drug Products during Storage and Transportation," Health Canada, April 28, 2011.

Handfield, Robert, "Major trends impacting the Pharmaceutical Supply Chain Ecosystem," North Carolina State University, Poole College of Management Blog, March 20, 2014.

Husten, Larry, "Pfizer Starts Testing for Over-the-Counter Lipitor," Forbes Magazine, March 2, 2014.

Knut, Alicke, Karrer, Christoph, Schrader, Ulf, "The Supply Chain: Where Push and Pull are Friends," PharmaManufacturing.com, December 30, 2010.

Kuzeljevich, Julia, "Health Canada reviews guidelines on distribution practices; says transport providers hesitate to sign quality agreements," Canadianshipper.com, February 27, 2013.

Latham, Cara, "Generics Outlook: Turning to Innovation after the Patent Cliff," Pharmacy Times, July l23, 2013.

"Learn About Counterfeit Drugs Around the Globe", Pharmaceutical Research and Manufacturers of America website, accessed October 21, 2014.

Leung, Philip, "Embracing China's Brave New Pharmaceutical World," Bain Brief, June 4, 2014.

Looser, Brian and Keenan, Stephanie, "Drug Quality and Security Act, What you Need to Know," McGuireWoods, December 4, 2013.

"Pharmaceutical Industry Profile," Industry Canada website, accessed October 23, 2014.

"Regulations Amending the Food and Drug Regulations (Retention of Records – Miscellaneous Program)," Canada Gazette, May 15, 2014.

Rockoff, Brian, "Goodbye Liptor. Pfizer Bids a Farewell," The Wall Street Journal, May 9, 2012.

"Safe Medical Devices in Canada," Health Canada website, accessed October 23, 2014.

"Transformation of the U.S. Medical Devices Supply Chain," Exel, 2013.

"Understanding the Drivers of Expired Pharmaceutical Returns," Healthcare Distribution Management Association, May 2009.

UPS Communications, "Pain in the (Supply) Chain Survey: Caution Remains in Health-Care Industry," 3PL Americas, International Warehouse Logistics Association, December 2012.

"UPS Survey: Time to Act on Untapped Opportunities in Healthcare Industry," UPS press release, September 23, 2014.

Wiener, Joshua and Tilly, Jane, "Population ageing in the United States of America: Implications for public programmes," International Journal of Epidemiology, Volume 31, Issue 4.