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# APPLICATIONS OF RFID IN THE PHARMACEUTICAL SUPPLY CHAIN


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# Introduction

The aim of this work is mainly to show the viable applications of the Radio Frequency Identification technology (RFID) inside the Pharmaceutical Supply Chain, by trying to understand the real scope of this technology in a complex and regulated industry as the pharmaceutical one.

This purpose will be addressed, by organising the thesis as follow.
In the first chapter it is explained the basics of RFID technology and discuss the current state of art in the standardisation of frequencies and hardware used. Then this section shows the main applications both in consumer and business-to-business context and in the end the main problems faced by a company in approaching this technology.
The second chapter describes the critical parties involved in the pharmaceutical industry from the manufacturer to the end-consumer, then examines the essential features of the pharmaceutical supply chain and the key concerns that this industry has to face to be really efficient and to deliver drugs in a safe, integrated and consistent manner.
In the last section, finally, the two predominant topics of the work are blended together, by examining how the RFID technology can be used inside the Pharmaceutical Supply Chain and the principal fields of application in the light of the main problems faced by this industry and described in the previous section.

The work does not want to look at the RFID technology as the panacea of all the issues inside this industry, but it want to try simply to fill a gap in the literature about the all possible uses of this technology inside the above mentioned industry.

# 1. PRELIMINARY KNOWLEDGE ABOUT RADIO-FREQUENCY IDENTIFICATION

Radio-Frequency Identification (RFID) technology is classified as a wireless automatic identification and data capture (AIDC) technology. AIDC technologies include barcoding, optical recognition, biometrics, card technology, touch or contact memory technology, and RFID technology. Some auto-ID technologies, such as barcode systems, often require a person to manually scan a label or tag to capture the data; RFID is designed to enable readers to capture data on tags and transmit it to a computer system—without needing a person to be involved.

Wireless technologies represent an emerging area of growth and are important even in mobile commerce (m-commerce) applications. Even though the terms ‘‘mobile’’ and ‘‘wireless’’ are used interchangeably, they actually have different meanings. Mobile means positioning a mobile device as any terminal that can be used on the move, while wireless refers to the transmission of data over radio waves, meaning that a wireless device is any terminal that uses a wireless network to either send or receive data.

Wireless networks can be divided into four main categories:

- Wireless Personal Area Network (WPAN), which can be used to allow PCs, PDAs, mobile phones to detect each other and interact;
- Wireless Local Area Network (WLAN), which provides simple Internet or intranet access to PCs, PDAs, and laptops equipped with a wireless network card;
- Wireless Metropolitan Area Network (WMAN); and
- Wireless Wide Area Network (WWAN), which is a location technology based on a system of satellites orbiting the earth (S. F. Wamba, 2008).

Radio-frequency identification (RFID) is a generic term that is used to describe a system that transmits the identity (in the form of a unique serial number) of an object or person wirelessly, using radio waves [3]. This information is transferred data from an electronic tag, called RFID tag, attached to an object, through a reader for the purpose of identifying and tracking the object. The tag's information is stored electronically.

RFID is a semiconductor-based technology that can be used to identify objects. In its most basic design, an RFID tag can be thought of as a wireless barcode [9].

The basic premise behind RFID systems is that you mark items with tags. These tags contain transponders that emit messages readable by specialised RFID readers. A reader retrieves information about the ID number from a database, and acts upon it accordingly. RFID tags can also contain writable memory, which can store information for transfer to various RFID readers in different locations (Weinstein R., 2005).

The RFID tag includes a small RF transmitter and receiver. An RFID reader transmits an encoded radio signal to interrogate the tag. The tag receives the message and responds with its identification information.

RFID is a superior and more efficient way of identifying objects than manual system or use of barcode systems that have been in use since the 1970s. It is not necessary to "show" the tag to the reader device, as with a bar code. In other words it does not require line of sight to "see" an RFID tag, the tag can be read inside a case, carton, box or other container, and unlike barcodes RFID tags can be read hundreds at a time. Bar codes can only be read one at a time [9].

RFID systems have three fundamental capabilities.

First, RFID is a means to wirelessly identify people and objects; his ability to identify things without human manipulation is an important service delivery advantage. Consider, for example, a hospital patient. Nurses need to be able to verify the delivery of medicine to the patient, and it is an important advantage of RFID that this can be done 24/7 without disturbing the individual, who might be unable to communicate or simply resting. RFID can help nurses serve patients better by obviating the need to disturb the patient to access a barcoded label; instead RFID can be read wirelessly through materials.

The second fundamental capability of some RFID systems is to automatically generate data that can be used to track and locate tagged items; fundamentally most RFID systems generate information based on wireless communications between tags and readers that can be used to locate the tag either directly or indirectly.

A third fundamental capability that some RFID systems have is to sense the surroundings; some types of tags include a variety of environmental monitoring

capabilities, such as the ability to track the ambient temperature, which enables the tag to act as a mobile sensor to wirelessly collect information about its immediate environmental conditions (Geraldo Ferrer, 2010).

This technology enables organisations to deliver value-added applications related to the tracking and intelligent management of any entity tagged with an RFID chip.

The technology has been around for more than 50 years; however, it has not been widely used. Since 2003, when Wal-Mart announced its intention to introduce an RFID application, it has brought new business opportunities to many information companies. With both identification and tracking characteristics, RFID may dramatically change the organisation's capability to obtain real-time information about the location and properties of tagged objects, such as people or products (Shiou-Fen Tzeng, 2008).

Current research and development on RFID focus on the manufacturing and retail sectors to improve supply-chain efficiency and to learn more about consumer behaviour. Healthcare is believed to be its next home (Gunasekaran, 2005).

## 1.1 The hardware for RFID

Tags and readers are the main components of an RFID system. An RFID tag is often confused with an RFID label. A tag is a transponder mounted on a substrate. It can be embedded in packaging or stuck on with adhesive. An RFID label is a transponder sandwiched between a layer with adhesive and paper that can be printed on [1].

Basically, an RFID system is composed of three layers:

- a tag containing a chip, which is attached to or embedded in a physical object to be identified;
- a reader and its antennas that allow tags to be interrogated and to respond without making contact; and
- a computer equipped with a middleware application that manages the RFID equipment, filters data, and interacts with enterprise applications (Samuel Fosso Wamba, 2008).

An RFID reader typically has an RF front end that serves one or more antennas, an RF signal processor, an air-protocol processing engine that implements the air-protocol

message decoder/encoder and state machine and algorithms, and the network interface processor to communicate with the upstream network elements.

There are different types of reader designs based on different factors:

- Number of antennas: multiple (typically 4 to 8) antennas or a single integrated antenna (readers can have internal or external antennas);
- Processing complexity: data processing includes business intelligence (sometimes referred to as "smart" readers), or just RF intelligence (sometimes referred to as "thin" readers);
- Tag access functions: some perform all air-protocol operations (read, write, lock and kill tags), others just inventory the tags;
- Connectivity: Ethernet, serial, or wireless (Readers can also have input/output ports for connecting to external devices. An output port might connect to a program logic controller, conveyor sorter or other device controlled by the reader. Readers also have ports for connecting to a computer or network.)
- Number of digital I/O ports: none or multiple (typically 1-4).

In its simplest classification, radio-frequency identification (RFID) tags can be separated in two types: active (where the tag has a battery) or passive (where the tags do not have its own source of energy) (P. Krishna, 2007).

### 1.1.1 Active RFID Systems

Active tags are used on large assets, such as cargo containers, rail cars and large reusable containers, which need to be tracked over long distances (in a distribution yard, for example). They usually operate at 455 MHz, 2.45 GHz, or 5.8 Ghz, and they typically have a read range of 20 meters to 100 meters.

Generally, there are two types of active tags: transponders and beacons.

- Active transponders are woken up when they receive a signal from a reader. These are used in toll payment collection, checkpoint control and other systems. When a car with an active transponder approaches a tollbooth, a reader at the booth sends out a signal that wakes up the transponder on the car windshield. The transponder then broadcasts its unique ID to the reader. Transponders conserve battery life by having the tag broadcast its signal only when it is within range of a reader.

- Beacons are used in most real-time locating systems (RTLS), where the precise location of an asset needs to be tracked. In an RTLS, a beacon emits a signal with its unique identifier at pre-set intervals (it could be every three seconds or once a day, depending on how important it is to know the location of an asset at a particular moment in time). The beacon's signal is picked up by at least three reader antennas positioned around the perimeter of the area where assets are being tracked. It has been used in a variety of contexts to locate individuals, such as in amusement parks and in prisons. RTLS has been used in ports to facilitate the location of a specific container among thousands, and at automobile distribution centers to help finding a specific vehicle in the lot. Its use in manufacturing sites has helped locating individually tagged items that may be lost in a large job shop.

Active tags have a read range of up to 100 meters and can be read reliably because they broadcast a signal to the reader (some systems can be affected by rain). They generally cost from $10 to $50, depending on the amount of memory, the battery life required, whether the tag includes an on-board temperature sensor or other sensors, and the ruggedness required. A thicker, more durable plastic housing will increase the cost.
Active tags are not mass-produced in high volume and don't have problems with antennas detaching from the microchip because they are usually housed in protective plastic [2].

### 1.1.2 Passive RFID Systems

Passive RFID tags have no power source and no transmitter. They are cheaper than active tags and require no maintenance, which is why retailers and manufacturers are looking to use passive tags in their supply chains. They have a much shorter read range than active tags (a few centimetres to 10 metres). A passive RFID transponder consists of a microchip attached to an antenna. The transponder can be packaged in many different ways. It can be mounted on a substrate to create a tag, or sandwiched between an adhesive layer and a paper label to create a printable RFID label, or smart label. Transponders can also be embedded in a plastic card, a key fob, the walls of a plastic container, and special packaging to resist heat, cold or harsh cleaning chemicals. The

form factor used depends on the application, but packaging the transponder adds significantly to the cost.

Passive tags can operate at low frequency, high frequency and ultra-high frequency. Low-frequency systems generally operate at 124 kHz, 125 kHz or 135 kHz. High-frequency systems use 13.56 MHz, and ultra-high frequency systems use a band anywhere from 860 MHz to 960 MHz. Some systems also use 2.45 Hz and other areas of the radio spectrum.

Radio waves behave differently at each of these frequencies, which means the different frequencies are suitable for different applications. Low-frequency tags are ideal for applications where the tag needs to be read through material or water at close range (more about read range in a minute). As the frequency of radio waves is increased they start to behave more like light. They can't penetrate materials as well and tend to bounce off many objects. Waves in the UHF band are also absorbed by water. The big challenge facing companies using UHF systems is being able to read RFID tags on cases in the center of a pallet, or on materials made of metal or water.

The absence of battery allows passive tags to be smaller, simpler, and less expensive, which makes it a natural upgrade from barcode, with the benefit of carrying more information about the tagged item. Active tags, however, are bulkier and more expensive. The active design is generally selected when other tag capabilities are desired, in addition to item identification. There are also semi-passive tag has a battery to operate the microchip, and also uses backscatter to communicate with the reader. Such tags have a considerably longer read range than passive tags [2].

The cost of a passive tag depends on its frequency, the amount of memory, design of antenna and packaging around the transponder. The cost generally ranges from 20 cents for the simplest tags to several dollars for transponders embedded in a key fob or plastic housing, to protect the tag from heat, cold or chemicals. An RFID transponder ina thermal transfer label that can be used for printing bar codes is typically 40 cents or more.

## 1.2 Infrastructure Elements

The RFID infrastructure consists of the elements that manage the devices and tag data. Consumers of the data are the client network elements (typically end-user applications). The network elements between the tag and the clients form the channel that transports tag data to the applications, and convey tag operational commands to the RFID devices.
At a minimum, the RFID infrastructure comprises tags, readers, RNCs (Reader Network Controllers) and applications. In addition, other devices could also be in the network such as RFID/bar code readers, I/O devices (such as electric eyes, light stacks and actuators), bar code/smart label printers and applicators.
Typically, a reader transmits an RF signal in the direction of a tag, which responds to the signal with another RF signal containing information identifying the item to which the tag is attached, and possibly other data. The tag may also include additional field-writable memory store, and integrated transducers or environmental sensors for providing data such as the temperature or humidity of the environment. The reader receives the information and provides the tag data to the RNC which may do further processing before sending the data on to the applications (P. Krishna, 2007).

The maximum range over which the reader can communicate with the tag depends on the transmit power of the reader, the environment through which the RF signal travels, the presence of interference and the receive sensitivity of the reader. Losses due to signal attenuation and multi-path interference reduce the range. Attenuation is low or negligible for gases in the atmosphere, such as nitrogen and oxygen, and also for paper, cardboard and certain plastics. Materials like metal and liquids have a stronger attenuating effect depending on their thickness.

The Reader Network Controller (RNC) plays the role of the RFID infrastructure layer. It transforms a collection of autonomous readers and devices into a reliable and scalable network. RNC functionality includes real-time adaptive control and management of readers and devices, location-aware tag and sensor data processing.

*Infrastructure Functions*

The infrastructure comprises three interlocked communications paths:

- data processing (the Data path), that refers to the tag and sensor information collected by the readers and forwarded to the Reader Network Controller and applications;
- device management (Management path): important because in an enterprise diverse types of devices are deployed;
- device control and coordination (Control path): with the advent of sophisticated air-protocols, and deployments of large number of readers, the need for reader control and coordination in the architecture becomes important.

An RFID infrastructure must take in consideration:

- Reader operations: A reader performs either inventory or access operations on a tag population. Inventory means that using a singulation algorithm, the reader isolates a single tag reply and reads the EPC memory contents from the tag. Access is used to describe the further operation of writing and/or reading other memory regions on a tag. Although the communication between a reader and tag is local, the interference impact due to that local communication is global; reader-to-reader interference occurs when a reader picks up another reader's transmit signal at, or near, the same frequency.
- Tag data processing: there is a phenomenon, which does not yet have a consistent name (it's been called "unwanted reads") and it is relates to the most fundamental difference between RFID and optical-bar-code technology (that it is replacing): the inability to know precisely which among the tags that a reader reads are the intended tags, and which are not. The optimal approach to eliminating unwanted reads is to rely on information such as the spatial relationships between the antennas and their locations, the read rates of the antennas, and the tags observed by the antennas.
- Device management and monitoring: There may be little or no onsite IT support for networked RFID readers deployed in environments. In such situations, automated configuration and discovery of the RFID readers and devices as they are set up is essential. Once they are set up, RFID system administrators will need device management and monitoring tools, health and performance monitoring, and firmware management of the readers and other devices in the infrastructure, will be critical.

– Inter-enterprise and intra-enterprise tag data and event dissemination: The tag data collected and the business events generated by the infrastructure need to be disseminated for closed-loop, open-loop and cross-enterprise data collection. This data exchange can involve many processes and potentially many companies (P. Krishna, 2007).

## 1.3 Middleware and Servers

Middleware is a generic term used to describe software that resides between the RFID reader and enterprise applications. It's a critical component of any RFID system, because the middleware takes the raw data from the reader, filters it and passes on the useful event data to back-end systems. Middleware plays a key role in getting the right information to the right application at the right time.

There are many RFID middleware products on the market. All do some basic filtering, but many also perform additional functions. Some middleware manages RFID readers: monitors their health, configures them, and sends software updates and so on. Some middleware has its own applications, often for a specific industry. One application might be confirmation of shipment and receipt. When a product is sent to a retailer, the middleware confirms the shipment and sends an electronic message to the retailer with the EPCs in the shipment. When the retailer receives the goods, receipt is confirmed and a message is sent to the supplier. The cost of middleware varies from vendor to vendor and is usually based on the number of locations where it will be installed, the complexity of the application and many other factors.

Companies will also need to purchase servers to run middleware within a warehouse, distribution centre or production facility. These servers are sometimes called edge servers. Edge servers are standard computer servers. They typically do not have any special hardware, and they connect to readers using serial or USB ports [1].

## 1.4 EPCglobal Network Infrastructure

EPCglobal is leading the development of industry-driven standards for the Electronic Product Code (EPC) to support the use of Radio Frequency Identification (RFID) in today's networks.

The Electronic Product Code (EPC) is designed as a universal identifier that provides a unique identity for every physical object anywhere in the world, for all time. The canonical representation of an EPC is a Uniform Resource Identifier (URI). The EPCGlobal Tag Data Standard defines the structure of the URI syntax and binary format, as well as the encoding and decoding rules to allow conversion between these representations. EPC is not designed exclusively for use with RFID data carriers. The EPC is designed to meet the needs of various industries, while guaranteeing uniqueness for all EPC-compliant tags.

The EPC Tag Data Standard defines the general data format for EPC number. In order to incorporate the globally accepted standards of all sectors, the EPC Tag Data Standard provides a structured, hierarchical numbering scheme in which the EPC is a numerical string comprised of several distinct segments. Three of those segments, the EPC Manager Number, Object Class and Serial Number, are relevant to this discussion:

- EPC Manager Number: EPCglobal issues a unique identifier, called the EPC Manager Number, to each EPC Manager to identify that member within the EPCglobal Network, regardless of industry sector or geography. The integration of the EPC Manager Number as a segment on the EPC string avoids fragmentation by enabling trading partners from any industry sector to be joined together in the EPCglobal Network.
- Object Class: The Object Class segment identifies the type of product to which the EPC is attached (e.g., a bottle of medication).
- Serial Number: The Serial Number segment identifies a specific instance of the object class (e.g. this specific bottle of medication). In order to enable EPC Managers to assign new EPCs without the possibility of collision with EPCs issued by other EPC Managers, the EPC Tag Data Standard nests the Serial Number segment beneath the EPC Manager Number and Object Class (EPCglobal US COMMENT DHHS ANTI-COUNTERFEIT DRUG INITIATIVE WORKSHOP) .

Figure 1: The structure of a 96-bit EPC ("Design and development of a mobile EPC-RFID-based self-validation system for product authentication",S.K. Kwok, Jacky S.L. Ting, Albert H.C. Tsang, W.B. Lee, Benny C.F. Cheung, 2010).

The AutoID Center, headquartered at MIT and working in conjunction with industry leaders and academic institutions around the world, designed a system for bringing the

benefits of RFID to the global supply chain. That system is referred to as the EPCglobal Network.

The vision of the Auto-ID Center was to have a global network infrastructure, a layer integrated with the Internet that would enable companies to look up basic information about items as they moved through the global supply chain. Companies that want to take advantage of this open network will have to purchase servers to host local Object Name Service directories. ONS is similar to the Domain Name Service that points computers to Web sites. ONS will point computers to Internet databases where data associated with an EPC are stored. The ONS has a distributed architecture, like the DNS. But companies will want to host a local ONS to avoid having to go out to the Internet to look up information about products every time they read a tag.

By using standards-based, EPCglobal-certified hardware and software components and interfaces, end users are assured that their EPC implementations and systems are compatible with their trading partners, enabling them to capture, store, and share EPC-related data up and down the supply chain.

The EPCglobal Network uses RFID technology to capture data and Internet technology to share and discover data. To capture EPC data, EPC tags carrying a globally unique EPC identifier are affixed to containers, pallets, cases, and/or individual units. Then, EPC readers at strategic points throughout the supply chain read each tag as it passes and communicate the EPC number with the time, date, and location of the read. That read event is then registered and stored at the local read site. Once the EPC data are captured, Internet technology is used to share that EPC data among authorised trading partners in the global supply chain. When a trading partner queries the network for information about an EPC, the query is directed to the location where information related to that EPC can be found. From there, various security services, including authorisation and access control, are performed before access is granted to the requested EPC information (Celeste Robert, 2006).

## 1.5 The frequencies used for communicating

There is no global public body that governs the frequencies used for RFID. In principle, every country can set its own rules for this.

Low-frequency (LF: 125–134.2 kHz and 140–148.5 kHz) (LowFID) tags and high-frequency (HF: 13.56 MHz) (HighFID) tags can be used globally without a license. Ultra-high-frequency (UHF: 868–928 MHz) (Ultra-HighFID or UHFID) tags cannot be used globally as there is no single global standard. In North America, UHF can be used unlicensed for 902–928 MHz (±13 MHz from the 915 MHz center frequency), but restrictions exist for transmission power. In Europe, RFID and other low-power radio applications are regulated by ETSI recommendations, allowing RFID operation with somewhat complex band restrictions from 865–868 MHz. Readers are required to monitor a channel before transmitting ("Listen Before Talk"); this requirement has led to some restrictions on performance, the resolution of which is a subject of current research.

In order to ensure global interoperability of products several organisations have setup additional standards for RFID testing.

Among groups concerned with standardisation there is EPCglobal - this is the standardisation framework that is most likely to undergo International Standardisation according to ISO rules as with all sound standards in the world. Currently the big distributors and governmental customers are pushing EPC heavily as a standard well-accepted in their community, but not yet regarded as for salvation to the rest of the world [9].

## 1.6 Application of RFID

In 2010 three key factors drove a significant increase in RFID usage: decreased cost of equipment and tags, increased performance due to an higher level of reliability, a stable international standard around UHF passive RFID thanks to EPCglobal.

RFID is becoming increasingly prevalent as the price of the technology decreases.

This section has not the aim of illustrating all the possible application of RFID, but most of them and the most important and impactive.

### 1.6.1 Consumer Applications of RFID

The most relevant applications of RFID in all-day life are the following [9]:

- Electronic vehicle registration: with security of cars being a major concern in many countries, some countries are using RFID technology for vehicle registration and enforcement. RFID can help detect and retrieve stolen cars. RFID is also being used to secure assets. A transponder is embedded in the plastic housing around the base of the key. Keys for new cars also incorporate passive RFID tags that work with a reader near the car's ignition switch. The reader will only accept codes stored in certain keys. If the code in a key does not match the reader in the car, the car will not start, making it more difficult to steal vehicles by copying keys.
- Payment without contact: MasterCard and Visa are experimenting with RFID to give consumers the convenience of paying for small purchases with a wave of a contact-less smart card or key fob. These are a replacement for identification cards with magnetic stripes, providing a more reliable way to store identification information (magnetic stripes tend to wear out and lose information over time). RFID tags also have a higher memory capacity than magnetic stripes.
- Payment by mobile phones: two credit card companies have developed specialised microSD cards. After inserting the microSD, a user's phone can be linked to bank accounts and used in mobile payment. For example, 7-Eleven has been working to promote a new touch-free payment system. Now, thanks to these applications, most phone manufacturers are creating phones with RFID capabilities: credit card information can be stored, and bank accounts can be directly accessed using the enabled handset.
- Transportation payments: Public transit (bus, rail, subway).
- Toll road.
- Bicycle Parking Facilities**:** Some bike hirers are operated with RFID cards assigned to individual users. A prepaid card is required to open or enter a facility or locker and then used to track and charge based on how long the bike is parked.
- Product tracking: RFID used in product tracking applications begins with plant-based production processes, and then extends into post-sales configuration management policies for large buyers. RFID can also be used for supply chain management in the fashion industry. The RFID label is attached at the garment at

production, can be read/traced throughout the entire supply chain and is removed at the point of sale (POS) because of privacy concerns.

- Animal identification.
- Hospital and Healthcare: Adoption of RFID in the medical industry has been widespread and very effective. Hospitals are among the first users to combine both active and passive RFID technology.
- Libraries: RFID tags used in libraries: square book tag, round CD/DVD tag and rectangular VHS. This technology has slowly begun to replace the traditional barcodes on library items, the RFID tag can contain identifying information, such as a book's title or material type, without having to be pointed to a separate database. The Dutch Union of Public Libraries is working on the concept of an interactive "context library", where borrowers get a reader set, which leads them to the desired section of the library and which they can use to read information from books on the shelves with the desired level of detail, coming from the book's tag itself or a database elsewhere, and get tips on alternatives, based on the borrowers' preferences, thus creating a more personalised version of the library.
- Passports: The first RFID passport (e-passport) were issued by Malaysia in 1998. In addition to information also contained on the visual data page of the passport, Malaysian e-passports record the travel history (time, date, and place) of entries and exits from the country. In 2006, RFID tags were included in new US Passport.
- Schools and universities: School authorities in the Japanese cities are now chipping children's clothing, back packs, and student IDs in a primary school. A college in London, started September, 2008, is using an RFID card system to check in and out of the main gate, to both track attendance and prevent unauthorised entrance.
- Museums: RFID technologies are now also implemented in end-user applications in museums. A visitor entering the museum receives an RF Tag that could be carried as a card, that enables the visitor to receive information about specific exhibits.
- Ski resorts have adopted RFID tags to provide skiers hands-free access to ski lift. Skiers do not have to take their passes out of their pockets.
- Human implants: Implantable RFID chips designed for animal tagging are now being used in humans. Security experts have warned against using RFID for authenticating people due to the risk of identity theft.

- Telemetry: Active RFID tags also have the potential to function as low-cost remote sensors that broadcast telemetry back to a base station.

### 1.6.2 Industrial applications of RFID

RFID applications are numerous and comprehensive. The most interesting and widely used industrial applications include those for asset tracking, supply chain management, manufacturing, security, movement tracking, product recalls and retailing (Geraldo Ferrer, 2010).

#### Asset Tracking

Companies can put RFID tags on assets that are lost or stolen often, that are under-utilised or that are just hard to locate at the time they are needed.

Logistics and transportation are major areas of implementation for RFID technology. For example, yard management, shipping and freight and distribution centres are some areas where RFID tracking technology is used. Transportation companies around the world value RFID technology due to its impact on the business value and efficiency.

For example, a third-party logistics provider may need to track containers in its distribution centres.

Air companies may need to track food carts used at airports around the world so to save great part of their expenditures: by placing active transponders under the carts and readers on the entrance and exits of catering facilities. They can not only loose fewer carts and spend less time and money taking inventory, they also are able to better manage the movement of carts.

Another application is the baggage tracking, in the Hong Kong International Airport, the luggage is individually tagged with an RFID tags as they navigate the airport's baggage handling system, which improves efficiency and reduces misplaced items.

#### Supply chain management

RFID technology has been used in closed loop supply chains or to automate parts of the supply chain within a company's control for years. In supply chain management, RFID tags are used to track products throughout the supply chain: from supplier delivery, to warehouse stock and point of sale.

As standards emerge, companies are increasingly turning to RFID to track shipments among supply chain partners. New applications target tracking from checkout through customer billing. A central database records product movement, which manufacturers or retailers can later query for location, delivery confirmation.

For this application, RFID basically serves as a replacement for the bar code scanners used to track products and shipments in similar ways. RFID is superior to bar codes for tracking inventory flow over the supply chain:

- RFID does not require line-of-sight access to read the tag.
- The read range of RFID is larger than that of a bar code reader.
- Readers can simultaneously communicate with multiple RFID tags. Because of this capability, an RFID reader can capture the contents of an entire shipment as it is loaded into a warehouse or shipping container. A reader collects detail information in one pass, without having to scan each product.
- Tags can store more data than bar codes.

The last capability has several interesting applications in supply chain management. For example, read-write tags can store information about their environment. They can physically store their position and time throughout their movement in the supply chain.

An example of a proposed use of RFID is to ensure safety in the supply chain. A US Food and Drug Administration (FDA) proposal supports using RFID to ensure the authenticity of prescription drugs. In this system, each drug shipment would carry a read-only RFID tag containing a unique serial number. Suppliers would track these serial numbers in shipment and have the drug purchaser verify the numbers on receipt, ensuring that the drugs came from where they were expected and arrived at their intended point of sale.

Inventory systems

A correlation to the supply chain management application is to enable automated just-in-time product shipments. If all products in a retail store and associated warehouses have RFID tags, a store should have an accurate database of its inventory. Systems in retail outlets could automatically alert a warehouse management system that inventories are low. An advanced automatic identification technology based on the Radio Frequency Identification (RFID) technology has significant value for inventory systems. Notably, the technology provides an accurate knowledge of the current inventory.

At Wal-Mart, RFID reduced out of stocks by 30 percent for products selling between 0.1 and 15 units a day. Other benefits of using RFID include the reduction of labor costs, the simplification of business processes, and the reduction of inventory inaccuracies.

RFID combined with mobile computing and Web technologies provide a way for organisations to identify and manage their assets. Mobile computers, with integrated RFID readers, can now deliver a complete set of tools that eliminate paperwork, give proof of identification and attendance. This approach eliminates manual data entry.

Web based management tools allow organisations to monitor their assets and make management decisions from anywhere in the world. Web based applications now mean that third parties, such as manufacturers and contractors can be granted access to update asset data, including for example, inspection history and transfer documentation online ensuring that the end user always has accurate, real-time data.

## Manufacturing

RFID has been used in manufacturing plants for more than a decade. It's used to track parts and work in process and to reduce defects, increase throughput and manage the production of different versions of the same product.

Boeing has been using an RFID system at it Wichita, Kansas, facility to track parts as they arrive, and as they move from one shop to another within the facility. In the past, bar codes associated with parts had to be scanned manually when a part went to an area in order to have a special chemical treatment. Then it had to be scanned out again. If a part wasn't scanned, the company lost track of it. Now RFID tags track the movement of parts automatically, reducing errors and the need to have people look for parts needed on the manufacturing line.

## Security

RFID has long been used as an electronic key to control who has access to office buildings or areas within office buildings. Security and personal identification applications are a major and broad application of RFID. A common use of RFID is in identification cards to control building access. Many organisations use RFID tags embedded in ID cards, which are readable at a building entrance.

After the terrorist attacks on New York and Washington, D.C., in 2001, the U.S. Department of Transportation (DOT) conducted a number of tests of RFID seals to safeguard containers. Seals are active RFID tags that have a mechanism for sealing a container. If the container is opened without authorisation, that information is communicated to a computer the next time the RFID tag in the seal is read. Then, a warning can be sent and agents can check the container.

### Movement tracking

Because moving objects can easily carry RFID tags, a common use is to track the movement of people and the information associated with them. Some hospitals now use tags, to ensure identification and to alert hospital staff should someone attempt to take the baby outside of the hospital without authorisation. Some schools are requiring children to wear tag-embedded bracelets or wrist bands while on school grounds, to monitor attendance and to locate lost children. The FDA recently approved a RFID tag that could stay with surgical patients in hospitals and store information on the surgical procedure the person requires, eliminating surprisingly common surgical mistakes. This application of RFID has obvious privacy issues.

### Product recalls

One area of importance is product recalls. Today, companies often need to recall their products, (e.g., meat or drugs) if there is a problem to ensure people's safety. But they can never be sure they recovered all the bad goods that were released into the supply chain. With RFID, companies will be able to know exactly which items are bad and trace those through to stores. Customers that register their products could be contacted individually to ensure they know something they bought has been recalled.

### Retailing

Retailers such as Tesco and Wal-Mart are in the forefront of RFID adoption. These retailers are currently focused on improving supply chain efficiency and making sure product is on the shelf when customers want to buy it.

Metro in Germany and Tesco in the United Kingdom have done extensive testing to see if putting RFID tags on individual products in the store can will help them to reduce out

of stocks. And Hewlett-Packard is tagging printers and electronic scanners shipped to Wal-Mart's Texas distribution centres. But given current tag costs (20 cents to 50 cents or more) it's likely to be several years before RFID has a big impact on retailing.

Among the most talked about potential applications are the ability to automate the checkout process and eliminate lines and the ability to market to consumers who opt in to loyalty programs while they are making purchasing decisions. Experts envision people putting items into a shopping cart equipped with a computer, small display and RFID reader. When checking out, the consumer walks through a tunnel reader, has all the items in the car read automatically and pays with the swipe of contact-less credit card. These applications require tags to be on virtually all items in the store, something that won't happen for at least a decade [9].

## 1.7 Challenges and issues in RFID

Even if this technology has a great impact on many applications, RFID is not without its challenges, which arise from both a technological and usage point of view.

### Privacy concerns

A common concern with RFID is privacy. It is disconcerting for many people to have their movements or buying habits automatically tracked electronically. Many privacy groups are concerned about the ability to identify people as they walk through a store or shopping centre via the tags embedded in their clothing and linked to them at the time of purchase.

To counter such concerns, RFID proponents propose that retail tags have “kill switches” that disable the tag at the point of sale. Even though a small tag might remain embedded inside a product, once the kill switch is activated, the tag would no longer transmit information.

The read range of RFID tags is much too small to allow readers out of personal range to read tags carried on a person or in a vehicle, and materials, all around us, tend to absorb the relatively weak RF waves transmitted by passive tags, making it extremely difficult to pick up RFID signals through the walls of a home. However, privacy concerns are very real.

Companies and government agencies must address these concerns before the public will truly feel comfortable using RFID systems. People will want to see policies about the use of an RFID system and the information it collects (Weinstein R., 2005).

### Security

Security is another key issue in RFID. An organisation that implements RFID in its supply chain does not want competitors to track its shipments and inventory.

People who use devices that carry personal financial information, such as credit card or other ID numbers, do not want others to access their accounts. These are significant security vulnerabilities in RFID.

Some researchers have proposed schemes that would require tags to authenticate readers, transmitting information only to authorised readers. The tags would have to store ID numbers for authorised readers, and a reader would have to broadcast its ID to the tag (Weinstein R., 2005).

### Integration with legacy systems

Another challenge to RFID is its integration into existing systems. Several vendors are developing RFID middleware that will link new RFID systems into existing back-end infrastructures. If an organisation picks a standard that changes or loses its market prevalence, middleware can transform the data from readers into the format supported by back-end systems. Middleware can provide the primary link between RFID readers and databases (Weinstein R., 2005).

# 2. PHARMACEUTICAL SUPPLY CHAIN

The aim of this chapter is to introduce the main components of the pharmaceutical supply chain and their principal features, then the section tries to synthesise the most important characteristics of the industry, and in the end the main problems faced by this industry are reported.

## 2.1 Components of the pharmaceutical industry manufacturing and distribution chain

The pharmaceutical supply chain is the means through which prescription medicines are delivered to patients.

The pharmaceutical supply chain is different in its organisation from all the other kinds of supply chain. To start with, there are the big pharmaceutical companies who manufacture prescription drugs. Then the next stages in this distribution chain are the large wholesalers who buy in bulk quantities. They then supply these drugs at varying prices to big traders, regional distributors, national level pharmacy chains and large retailers like, as well as to hospitals.

Between these entities, there are the large logistics service providers, warehousing companies and transporters who physically ship these drugs. Hence your corner pharmacy may have received its stock through at least two or three intermediaries with plenty of stops in between, where the drugs may be handled. Up to now, this is similar to the movement of consumer goods.

This is where the similarity ends. For the pharmaceutical business, the pricing for each end user is different. Therefore a typical hospital gets these drugs at lower rates than does a corner pharmacy. The pharmaceutical supply system is complex, and involves multiple organisations that play differing but sometimes overlapping roles in drug distribution and contracting. This complexity results in considerable price variability across different types of consumers, and the supply chain is not well understood by patients or policymakers [10].

There are many variations on this basic structure, as the players in the supply chain are constantly evolving, and commercial relationships vary considerably by geography, type of medication, and other factors.

A typical pharmaceutical supply chain will consist of the one or more of the following nodes (John V. Gray, 2011):

- primary manufacturing (possibly including contractor sites);
- secondary manufacturing (possibly including contractor sites);
- market warehouses/distribution centres;
- wholesalers; and
- retailers (pharmacies)/hospitals.

Figure 2: The main actors in the pharmaceutical supply chain (karbassi, 2009)

### 2.1.1 Manufacturers

Manufacturers are the source of the prescription drugs in the pharmaceutical supply chain. The pharmaceutical manufacturing industry is composed of two distinct business models: manufacturers of brand-name drugs (e.g., Pfizer, Merck, and Novartis) and manufacturers of generic drugs (Anonymous, 2005).

There are few pharmaceutical companies that participate in both the branded and generic parts of the industry, and both models focus on the manufacturing and packaging of pharmaceutical products, but there are other important differences. Most brand manufacturers devote a portion of their expenses to the scientific research and development of new drug therapies. Generic drug manufacturers typically do not develop new drug therapies, but instead manufacture generic compounds, that compete directly with the original branded version of a drug once the brand product's patent protection has expired.

Manufacturers manage the actual distribution of drugs from manufacturing facilities to drug wholesalers, and in some cases, directly to retail pharmacy chains, mail-order and specialty pharmacies, hospital chains, and some health plans. Manufacturers may also distribute products directly to government purchasers, which typically receive the largest price discounts. Wholesale distributors are the manufacturers' largest purchasers. Very few drugs are distributed directly to consumers.

Manufacturers also play roles in stimulating demand for drug products:

- through underwriting clinical studies designed to demonstrate the value proposition of pharmaceutical treatments compared to one another or compared to no clinical treatment at all;
- by engaging in the promotion and marketing of products to health care providers and direct-to-consumer advertising; and
- by administering patient assistance programs that provide the firm's products at nominal cost to low-income consumers.

Manufacturers also play an important role in ensuring the safety of the pharmaceutical supply chain by producing informational labelling for prescribers and consumers , and by using electronic bar-coding technology on drug packaging that may be used to track individual production lots, and to prevent prescribing errors.

## Primary manufacturing

The primary manufacturing site is responsible for the production of the active ingredient. This normally involves either several chemical synthesis and separation stages to build up the complex molecules involved, or fermentation and product recovery and purification in the case of biochemical processes (Shah Nilay, 2004).

The manufacturing process is characterised by long task processing times, often rounded to multiples of shifts. Where multistage processes are operated, considerable inventories are often held between stages. Furthermore, material from an intermediate stage must often pass some form of quality control check before being approved for use downstream in the process. This can introduce additional delays into the system.

The traditional process technology involves batch equipment and flexible pipework. The relatively low production volumes result in multipurpose plants to spread the capital cost between products. The need to avoid cross-contamination of products and requirements for validated cleaning and changeovers results in long downtimes between products.

A further source of complexity (and convenience) is the use of contractors to manufacture some or indeed all of the active ingredient stages. This process of outsourcing is a growing one, as research-oriented companies concentrate on the discovery and development activities and rely on third parties' manufacturing competence. This gives rise to extended supply chain co-ordination problems.

The production volumes are low, transportation costs are not significant at this stage of the supply chain, so primary sites may be located anywhere in the world, even distant from secondary manufacturers. The factors limiting the choice of location will be tax rates, existence of skilled working force, political and economic stability etc.

### Secondary manufacturing

The secondary manufacturing is concerned with taking the active ingredient produced at the primary site and adding “excipient” materials along with further processing and packaging to produce the final products. An excipient is generally a pharmacologically inactive substance used as a carrier for the active ingredient of a medication. In many cases, an "active" substance may not be easily absorbed by the human body; in such cases the substance in question may be dissolved into or mixed with an excipient (Shah Nilay, 2004).

For example, a product that is sold in pill form would undergo:

(i) granulation: with addition of all the excipient materials;

(ii) compression: forming the pills;

(iii) coating;

(iv) quality control; and

(v) packaging.

There are often many more secondary manufacturing sites than primary ones, serving local or regional markets. Transportation between sites is of the order of 1 or 2 weeks if by ship (usually the default mode) and of the order of one or two days if by air.

Figure 3: The sequential phases of the serial production process.

## 2.1.2 Wholesalers

Wholesale distributors purchase pharmaceutical products from manufacturers and distribute them to a variety of customers, including pharmacies (retail and mail-order), hospitals, and long-term care and other medical facilities (e.g., community clinics, physician offices and diagnostic labs).

Some wholesalers sell to a broad range of potential clients while others specialise in sales of particular products (e.g., biologic products) or sales to particular types of customers (e.g., nursing homes).

In the past, wholesalers limited their operations to a traditional distribution function. They provided the link between manufacturers and pharmacies by warehousing products and managing inventory. While "traditional" distribution services remain the cornerstone of the business, the industry has developed a more comprehensive list of services in response to the evolving marketplace, like: specialty drug distribution, drug repackaging, electronic order services, reimbursement support, and drug buy-back programs (Anonymous, 2005).

Figure 4: The structure of the pharmaceutical supply chain. (RFID systems for pharmaceutical distributors to meet the new FDA regulations on drugs, Abhisam, Pharma 2020)

Wholesalers play a significant role in this sector. They tend to be large and few. About 80% of demand flows through this channel in the UK (with three large players

accounting for almost all the demand), with the large part of the remainder going to hospitals. The wholesale distribution industry has consolidated in the last 30 years, with the number of wholesale distributors in the U.S. declining from approximately 200 in 1975 to fewer than 50 in 2000 (Shah Nilay, 2004).

### 2.1.3 Pharmacies

Pharmacies are the final step on the pharmaceutical supply chain before drugs reach the consumer. Pharmacies purchase drugs from wholesalers, and occasionally directly from manufacturers, and then take physical possession of the drug products.

After purchasing pharmaceuticals, pharmacies assume responsibility for their safe storage and dispensing to consumers.

Pharmacy operations include:

- maintaining an adequate stock of drug products,
- providing information to consumers about the safe and effective use of prescription drugs, and
- facilitating billing and payment for consumers participating in group health benefit plans.

Pharmacies also serve as a vital information link between drug manufacturers, and wholesale distributors. Unlike most other sectors of the health care delivery system, the pharmaceutical supply chain is highly automated and virtually all claims transactions are handled electronically, rather than on paper. Pharmacies are not only as the final point of sale for pharmaceuticals, but also as an interface between the supply chain and the consumer. Because of this secondary function, they also generate information on prescription drug claims and health plans. Other types of information, both quality-focused (e.g., drug-drug interaction warnings) and utilisation management-based (e.g., formulary compliance messaging) can originate from other parts of the supply chain, to the pharmacy as a prescription is being dispensed. As the final actor in the supply chain, it is up to the pharmacy to take action based on the information provided.

There are several types of pharmacies, including independent pharmacies, chain drug stores, pharmacies in supermarkets and other large retail establishments, and mail-order pharmacies. Most pharmacies purchase their drug supply from a wholesale distributor, although in some cases, large institutional and retail chain pharmacies, specialty pharmacies, and mail-order pharmacies obtain drugs directly from a manufacturer. Once a pharmacy takes possession of the drug products, it distributes the products to physicians or directly to consumers. In addition, there are specialty pharmacies, which specialise in the distribution of high-cost and more complex drug therapies.

In addition to traditional retail pharmacy services, consumers have increasingly been using specialty and mail-order pharmacies over the past several years. Growth in the use of these types of pharmacies is expected to increase rapidly in the future.

The main types of pharmacies are here listed, except for the traditional ones:

- Specialty pharmacies serve patients with chronic diseases by dispensing high-cost biotechnology drugs. The specialty pharmacy industry today is dynamic, with new companies entering continuously. Types of firms in the market range from publicly-traded stand-alone firms to retail pharmacies, and home health companies.
- Mail-order pharmacies receive prescriptions by mail, fax, phone, or Internet at a central location; process the prescription in large, mostly automated centres; and mail the prescribed drugs back to the consumer.
- Long-term care pharmacies, sometimes called institutional pharmacies, are a third type of specialised retail pharmacy. Long-term care pharmacies address the special needs of nursing homes, providing packaging for controlled administration, and special services that are more extensive than those provided by retail pharmacies., like: quality assurance checks, emergency drug kits and medication carts, regular and emergency (24-hour-a-day) delivery services, and in-service training programs for nurse aides, nurses, and other professional nursing facility staff (Anonymous, 2005).

## 2.2 Main features of the pharmaceutical supply chain

In this section, a general overview of the pharmaceutical supply chain characteristics will be presented (Kamran Karbassi, 2009).

Inside this supply chain it's very important to get the product from the warehouse to the hospital as soon as possible, so the supply chain needs to be set accordingly to accommodate the need for the fast delivery of the product. In the pharmaceutical supply chain, this need for speed and delivery reliability is addressed by keeping excessive inventory at various warehouses.

This is even more important because of the social responsibility that this industry has to ensure by providing 100% product availability at the right time at the right cost and in good conditions to right consumer.

There is a general trend for companies to divest excess capacity that came about from having many local manufacturing sites, and move towards a global supply chain management process. This brings with it many complex coordination issues and much tighter capacity constraints. Currently, the logistic cost in the sector is relatively high.

In pharmaceutical supply chain, firms can gain flexibility by eliminating bottlenecks and having immediate access to advanced technologies; this would ensure responsiveness by meeting customer orders for special sizes, packaging or labelling and getting new product to the market as soon as they get approved. Therefore all the activities will need to be streamlined in order to gain the complete responsiveness and agility.

Probably the single most important driver in the pharmaceutical industry is the time-to-market. Companies secure very significant returns in the early life of a successful drug, before any competition. The competition-free life is shortening, typically from 5 to 1–2 years. Competition in this sense relates to similar (rather than exactly the same) drugs. For most pharmaceutical companies it takes 10 to 15 years to introduce a new drug to the market so the earlier a product arrives to the market the more competition-free life the product will have. It is important to describe the life-cycle of a drug; it is somewhat different from that of other process industry products.
The research or discovery phase tends to use thousands of more or less random test compounds against therapeutic targets. It typically takes about 10 years to result in a potential new drug that is registered. From this point onwards patent protection applies. The potential new drug must then be tested for both safety and efficacy.
This involves a variety of trials: early on for toxicity and later on for ability to alleviate symptoms and remove disease. Finally, the process development activity comes up with a chemical or biochemical route to manufacture and an associated manufacturing process. This set of activities typically takes 6–8 years and is usually known as the development activity.

Figure 5: Pharmaceutical product life cycle(The TRIPs Agreement and pharmaceuticals, 2000).

In pharmaceutical industry we have a push process from the manufacturing side, where the generic components would be manufactured according to the forecasts; instead on the other side, the process uses a pull strategy, because the national health service will be order from the pharmaceutical company according to the demand of the customers.

Companies in pharmaceutical sector should share the necessary data with key vendors and customers in order to avoid the order loss, miss delivery and obsolete inventory, and so to ensure the visibility inside the whole supply chain. Another key issue for the visibility is the need for tracing drugs and product information in order to manage the full life-cycle of products.

Anyway, the main issue of this industry is its regulations. Given the significant potential for adverse health effects, the industry is subject to very stringent regulations. This starts from the processes used to evaluate the safety and efficacy of the chemical compounds, through to the details of the process and plant design and manufacturing operations. It may be the case that the existence of regulatory protocols has hindered innovation in this sector; with companies blaming regulators for their own innate conservatism.

The regulatory process tends to be slow and expensive; both these effects must be considered by the industry. Furthermore, the complex chemical compounds involved have more complex manufacturing processes, and the activities of route investigation, process development, scale-up plant design, commissioning and qualification are either increasing in duration.

In pharmaceutical sector, so many regulatory bodies exist, affecting the supply chain and making this process very long and expensive. This is due to the high potential for adverse health effects and risk of fatality, so the government bodies need to influence this industry by controlling the patent issued, pricing the products, by controlling imports and exports, and by certifying the product and allowing the sales in the country.

In recent past, this industry has been subjected to an high quantity of changes. Among all we can list these following (Shah Nilay, 2004):

- R&D productivity (in terms of numbers of new chemical entities registered per unit amount of investment) is declining;
- effective patent lives are shortening;
- even while active, patents provide lower barriers to entry;
- there are many product substitutes in many therapeutic areas; either alternative compounds or off-patent generics; and
- the payers of healthcare are exerting strong price pressure and influencing prescribing practices; this means that in order to be approved, new drugs must address new therapeutic areas or have very significant cost or health benefits over existing treatments.

On the one hand, the global marketplace has become more liberalised, exposing products to competition. On the other, governments and other agencies have tended to intervene more as they become concerned at every increasing healthcare costs associated with ageing populations. Measures taken include strict controls on the prices of new drugs, more cost–benefit analysis, and encouragement of the use of generic substitutes or alternatives where possible.

## 2.3 Problems and key issues inside the pharmaceutical supply chain

Historically, most management attention has been paid to drug discovery and sales and marketing (the extreme ends of the supply chain), but now much more attention is being paid to supply chain optimisation as a means of delivering value. According to (Shah Nilay, 2004):

- there is a welcome move away from viewing the supply chain as merely having to deliver security of supply at minimum cost, to a recognition of its ability to generate both value for the customer and hence to the shareholder; and
- restructuring of the supply chain along regional and global lines will require massive reductions in capacity, which was acquired in many cases to propitiate national interest in return for sympathetic pricing.

The main problems faced by this industry are now reported.

### 2.3.1 Integrating the supply chain components

The supply chain components are primary sites (Active-Ingredient manufacturers) and respective storage facilities, secondary sites and respective warehouses and final product market areas.

Each primary site may supply the active ingredient to any of the secondary sites and be located in any place around the world. For secondary sites and markets, we consider several geographical areas. Since transportation costs are very significant at this end of the supply chain, material flows between two different geographical areas are not allowed (Rui T. Sousa, 2011).

It is relevant to make the following supply chain decisions:

- where to allocate the manufacture of primary and secondary products and how to manage the available resources during the whole time horizon;
- what production amounts and inventory levels should be set for each manufacturing site;
- how to establish the product flows between primary and secondary sites and between secondary sites and markets.

The company has to consider:

- production costs;
- transportation costs;
- inventory handling costs;
- products allocation costs;
- unmet demand costs;
- tax costs (Ruggero Golini, 2011).

### 2.3.2 Information flows

It is clear that pharmaceutical companies, positioned at the upstream part of health care value chain, have to carefully manage not only the upstream information flow, which carries demand data from the market, but also the downstream technical information flow, which helps creating demand (Marcelo Caldeira Pedroso, 2009).

A first view on how those companies organise their supply chain shows that they have developed two different paths: one, a material delivering path, where products, order

information and financial assets are conveyed, and a demand creating path, where technical information on drugs is delivered to physicians.

In the material delivering path, sell-in represents the product inflow to drugstores, and sell-out the product outflow to patients, which demand is generated by the physicians' prescriptions. Drugstore inventories account for the difference between sell-in and sell-out, and the ratio sell-in/sell-out for the effectiveness of inventory management of drugstores. Order information flows up-stream through the material delivering path, from customers to drugstores and eventually to pharmaceutical companies. Technical information flows downstream through the demand creating path, from pharmaceutical companies to physicians.

Both information flows are complex, possessing particular features, and hard to manage. All pharmaceutical companies start delivering technical information to the market long before the product reaches drugstore shelves.

As soon as a new molecule proves to be a potentially viable new commercial product and clinical trials reach the final stage (which can still take some years to be finished), pharmaceutical companies start working to build their technical information pipelines.

Figure 6: Sell-in, sell-out and demand generation in the pharmaceutical industry (M.C. Pedroso, D. Nakano / Int. J. Production Economics 122, 2009).

Pharmaceutical companies build multiple technical information pipelines. Since technical information is rich, and effectively delivering it implies interacting, discussing and clarifying questions. Rich information requires high capacity channels and it is much more effectively delivered by personal contact, so ICT-based systems play only a limited, supporting role.

The characteristics that the information inside the pharmaceutical supply chain should have are (Yao-Hua Tan, 2010):

- the information concerning the pharmaceutical product should flow with the product as the product moves through the supply chain and consumer environment;
- this information needs to be freely available to those that require it;
- this information needs to possess a high-level of integrity concerning its accuracy, and should only be able to be modified by authorised parties;

- lastly, this flow of information needs to be conducted in a manner that the privacy of all parties should be preserved and that the information should be provided to only those parties who are authorised for it. That is, any information that a consumer possesses drugs/medication can lead to discrimination. Consequently such information cannot be transmitted in public. If we use an RF signal to transmit information concerning pharmaceutical information then we must "hide it". The solution is to encrypt this information. Only an authorised party should be able to determine the identity of a drug through the RF contact. Some relative information of a drug may also need to be protected due to commercial privacy. Usually manufacturers do not want others to know inside products and processes that they employ.

Figure 7: Knowledge and information flows in pharmaceutical supply chain (M.C. Pedroso, D. Nakano / Int. J. Production Economics 122, 2009).

### 2.3.3 Inventory control

A pharmaceutical industry has the main objective of satisfying forecast demand for product end items by (Shawnee K. Vickery, 1985):

- Minimising backorders (a customer order that cannot be filled when presented, and for which the customer is prepared to wait for some time) for the current scheduling horizon;
- Minimising work-in-process and finished unit inventory levels;
- Minimising work-in-process inventory accumulations.

It is also important to reduce the cost of direct work inside the warehouse and speed up the inventory process. Most significant in the case of a pharmaceutical supply chain is to have a real-time inventory monitor within the manufacturing location, warehouse, and retail store.

### 2.3.4 Contamination and substitution of both active and inactive ingredient within the global supply chain

One trend in the pharmaceutical industry has been the global sourcing of both active and inactive ingredients from emerging economies where costs are lower. Further, the manufacture of generic drugs or those coming off patent are also more likely to be outsourced to manufacturers in developing countries (Ann Marucheck, 2011). For

example, in the last decade the value of India's production of both active ingredients and finished formulations for export has doubled. The long supply chain, with sourcing, manufacturing, packaging and distribution occurring in different locations globally, has increased the risks of contamination or substitution of alternative ingredients.

Risk control through governmental regulation and inspections may be ineffective in detecting all the risks that can occur at each point in a multi-tier supply chain, particularly when the contamination is intentional or when there is fraudulent certification that the product has met all regulations and passed inspection.

### 2.3.5 Counterfeiting and infringement inside the supply chain

Since the 1982 Tylenol deaths, public attention has been awakened to the vulnerability of pharmaceuticals in the supply chain (Ann Marucheck, 2011).

Pharmaceuticals are chemical substances used to diagnose, cure, treat or prevent disease or adverse medical conditions. They are among the most highly regulated of all products with many nations enforcing strict regulations on the marketing and sale of drugs. Since they are metabolised in the body, pharmaceuticals are subject to many of the same regulations found in the food industry, in fact the government body that decides these norms in US is the Food and Drug Administration.

However, since a drug must be proven safe and effective in fulfilling its intended medical purpose, the approval process contains additional controls such as medical and scientific review, as well as clinical patient trials, to empirically test its effectiveness within the population.

In medicine and the life sciences, drug safety means efficacy of the treatment, the absence of serious side effects, and the minimisation of any interactions with other drugs that the patient may be taking. In the actual cases of contamination the fake drugs have contained ingredients that were (David C. Wyld, 2008):

- inactive;
- incorrect;
- improperly dosed;
- sub-potent;
- super-potent;
- expired; and/or

- contaminated.

Given the complexity of the drug distribution system, achieving a closed distribution system is not an easy task. It has been estimated that there are approximately 80.000 dispensing sites, only in the United States, that are supplied by a shifting group of primary and secondary wholesalers. While 3 major drug distributors dominate the primary market, there is a much larger number of both licensed primary and secondary distributors.

Secondary buying and selling of packaged pharmaceuticals is common as a normal part of inventory adjustment; however, it is often the way in which counterfeit medicines have entered the US distribution system.

In addition, numerous Internet sites offer consumers pharmaceuticals at deeply discounted prices even though these products are of dubious origin and quality.

Repackaging of pharmaceuticals takes place at a variety of levels, removing the manufacturer's original container/closure system and any incorporated counterfeit-resistant features.

Collectively, all of the above practices may create opportunities for counterfeit or diverted drugs to enter the system, thus potentially compromising the public health of patients.

Companies already are beginning to employ counterfeit-resistant technologies into packaging and labelling for a number of products. Such technologies include overt and covert features incorporated into the packaging and/or labelling of the product and chemical tags incorporated into the drug product itself. Overt features include holographic images, special stickers, inks of gradated colours, or threads in the container label, all of which can be used to verify that the container is authentic.

The main reasons of such an unfortunate growth in counterfeit drugs are (David C. Wyld, 2008):

- the relative ease of it;
- the cost of prescription drugs;
- the web of country-specific regulations;
- the vast cost disparities between countries on products;

- the ease of transporting pharmaceuticals (which are generally shipped in cases, not pallets);
- the practice of relabelling, repackaging, and reimporting controlled substances;
- the low prospect of being caught once the counterfeit pharmaceuticals are integrated into the drug supply.

The result is risk to patients' health, either risk to their safety directly if the products are dangerous or risks from people suffering from complications from the many diseases that prescription drugs can treat today.

There is already evidence that counterfeit drugs are worsening public health in general around the globe. For instance, in many Southeast Asian countries, over half the drugs sold do not have the correct formulation or levels of the active ingredient. Recently, the toll of counterfeit drugs is mounting worldwide. Consider these recent news headlines from around the globe:

- Last year in Hamilton, Ontario, Canada, a registered pharmacist, was arrested by the Royal Canadian Mounted Police. He was working at a retail drug store, dispensed counterfeit doses of Norvasc to heart patients – pills filled with only talc. The local coroner investigated five patient deaths – all caused by a heart attack or stroke – that may have been brought about by the substitution of the counterfeit drug (Pitts, 2005).
- Within the last year, counterfeit versions of three popular drugs – Lipitor for cholesterol, Cialisw and Reductil have surfaced in England. One British expert has estimated that 100,000 counterfeit drug imports are dispensed by the UK's National Health Service annually (Eban, 2006).
- In China, a counterfeit drug smuggling ring was recently broken-up that involved almost a half-million fake pills, including Lipitor.

An important change, that contributes in the increase of counterfeiting phenomena is the increase of manufacturing outsourced activities, there are a number of unscrupulous manufacturers, many located in India, China and Southeast Asia, who will produce the counterfeit drugs and package them so they look authentic. Group purchasing organisations (GPOs) seeking lower costs for volume purchases may fall prey to

counterfeiters and bring them into hospitals and other health care organisations. Another source of counterfeiting includes hackers who breach the proprietary data of pharmaceutical corporations to steal formulas and logistics strategies. Finally, well-publicised shortages of drugs, like vaccines, may cause legitimate health care organisations to seek alternatives to name brand products and unintentionally procure counterfeit drugs.

*Consequences of counterfeiting*

Counterfeit drugs cost pharmaceutical companies an estimated $46 billion annually. Considering the fact that pharmaceutical companies expend sometimes hundreds of millions of dollars to develop new drugs, this is a hit directly on their profits.

Counterfeiters are able to offer a lower price point than the manufacturer and, therefore, pose an unfair competitive threat that can erode pharmaceutical company profits. Counterfeiting and other forms of intellectual property theft cost American businesses at least $250 billion annually and counterfeit drugs worldwide cost pharmaceutical companies as much as $46 billion annually. Moreover, industry metrics suggest that the counterfeit threat to profits is growing steadily (Alan Minsk, 2009).

In 2007, the government estimated that United States spending on pharmaceuticals would surpass $247 billion in 2008. As consumer spending increases, so does the incentive for counterfeiters for entering in the legitimate market.

Pharmaceutical companies also risk serious loss of consumer confidence as counterfeits become more prevalent, indeed the presence of counterfeit products in the market weakens legitimate brands, as when patients and doctors fail to see results from the use of what are unknowingly counterfeit products, they will be less likely to use or prescribe that brand of drug in the future.

Increasingly, counterfeiters are dealing in drugs that are vital to consumer health, such as drugs for hypertension and high cholesterol. A counterfeit scare involving such vital drugs could substantially reduce consumer confidence in certain drug companies and brands of drugs. Companies that make large investments in developing their goodwill with consumers and establishing a trademarked brand name and image that inspires confidence must be proactive in protecting this substantial investment.

### 2.3.6 The rise of secondary distributors

Another problem is the increasing number of secondary distributors; because of the complexity of the supply chain may grow. While not necessarily illegal, secondary distributors may present some safety risks. Secondary distributors represent another supply part in an already complex supply chain (Ann Marucheck, 2011).

They often purchase product from a source other than the manufacturer, such as another distributor, and then sell the product directly to a health care organisation or a customer. Often when manufacturers offer discounts to meet sales targets or to reduce their inventories, secondary distributors may begin to stockpile drugs and later sell and divert them back into the primary distribution system.

There are three possible safety problems related to this behaviour.

- One is that secondary distributors may stock-pile drugs that are near their expiration date and then introduce them back into the supply chain at lower prices.
- Second, the distributors may not have proper storage conditions for drugs that are sensitive to high temperatures and, thus, compromise the safety and effectiveness of the drug.
- Third, the distributors may stock-pile critical drugs and, if the drug is in short supply, they will enter the market with inflated prices. While there may be nothing illegal with this arbitrage behaviour, it is certainly unethical. It also leads to conditions where counterfeiters could easily enter the market and infiltrate the primary supply chain by offering the critical drug at cheaper prices and in abundant supply. Thus, some of the challenges associated with balancing supply with demand in the pharmaceutical supply chain can be traced back to the influence of the secondary distributors.

Because drug may be illicitly distributed like trafficking, a complete history (origination, transportation, distribution, usage and disposal) of a drug may be useful for tracing within a crime investigation. Each drug should have a reliable history record for lawful tracing.

### 2.3.7 Recall

The supply chain is described not only by the traditional forward flow, that links suppliers to customers through factories, warehouses and distribution centres, but also considers the existence of reverse flows where recycling or non-conforming products are returned to factories, for extra processing, or sent to disposal (A.C.S. Amaro, 2008).

As product recalls continue to increase, firms, regulators, investors, and consumers are gradually recognising that recalls are an inevitable part of conducting business. However, the recent spate of product recalls has shifted attention from why products are recalled to why it takes so long to recall a defective product that poses a potential safety hazard (Manpreet Hora, 2011).

For example, in a recent and by this time famous automotive recall in the U.S., Toyota recalled many of its makes and models because their gas pedals were getting stuck, which clearly posed potentially serious safety hazards.

Reduction of time to recall may be important for at least three reasons.

- First, the sooner the defective product is recalled after it is first brought to market, the more the firm may benefit from learning about the defect and take rapid remedial action. Furthermore, it may be subsequently easier to fix similar defects in related products before they are sold and in turn potentially reduce further external failure costs.
- Second, the recall effort and costs to withdraw the product will be lower if the recalled product is with the downstream supply chain intermediaries, such as a distributor or retailer, rather than in the hands of the end customers. As time to recall increases, so do the probability of additional defective product entering the marketplace, making recovery more challenging for the firm and thus increasing demand risk. For example, in 1982, Johnson & Johnson recalled 31 million units of Tylenol because of safety issues.
- Third, as the time to recall defective and/or unsafe products lengthens, the delay may cause numerous injuries and even deaths. In those cases, questions begin to be raised by the stakeholders about the delay, and restoring the lost reputation becomes more challenging for firms.

Processing recalls is a part of the reverse supply chain, as it requires logistical planning in order to take the product back and then dispose of it, repair it, or refund the purchase price.

The cumulative body of operations management research indicates a positive association between cost of good quality and performance. Firms adopting and implementing total quality management programs and winning quality awards show a positive association with both stock price and operating performance. Product recalls due to lack of safety highlight quality failures that can be expensive for the firm.

The magnitude of a recall's negative impact on performance varies by recall severity, firm size, and remedy to recall. Furthermore, costs of external failure are exacerbated if recalls related to lack of safety translate into incidents of product-harm crises such as injuries, deaths, and property damage - all of which may give rise to additional product liability charges linked reputation of firms with recalls and found that firms with a stronger reputation experience a higher reduction in their market value than do firms with a weaker reputation.

### 2.3.8 The outsourcing trend

Outsourcing has been defined by Chase et al. as an "act of moving some of a firm's internal activities and decision responsibilities to outside providers". Outsourcing is a broad phenomenon and it can cover many areas and industries. It's based on the idea of focusing on core competencies, because it has been recognised in the strategy literature as a critical success factor in the long-term survival of a company (Youssef Boulaksil, 2010).

As companies have outsourced manufacturing to lower cost countries around the world, there has been concern that pressures for lower costs, combined with the additional complexity of the supply chain, will continue to lead to safety problems.

An important issue is the relative benefits of vertical integration versus outsourcing with respect to safety. The high costs associated with supply disruption, product liability and potential recall might indicate that some low-cost suppliers are really high-cost suppliers when the expected costs of safety risk are considered.

A second question is how to coordinate and monitor the behaviour of suppliers with respect to product safety. For example, in the case of the Mattel toy recall, the company had developed a certification program and rigorous testing rules to make sure that its Chinese contractors adhered to standards for the allowable levels of lead in paint. Yet some subcontractors were careless, while others intentionally violated the rules.

Information technologies are increasingly being explored as tools for better coordination and monitoring of the manufacturing process to avoid quality and safety problems. These technologies can provide real-time monitoring of processes across a global supply chain that allows companies to manage supplier behaviour, especially suppliers located across the globe.

Even the FDA is taking a more collaborative approach and stressing education and training in its practices with foreign countries. Included in FDA's budgets for fiscal year 2010 were specific items designed to improve product quality and safety in the medical device industry. For example, it proposed to provide onsite training to foreign regulators on medical device safety and quality (Ann Marucheck, 2011).

In the pharmaceutical industry, there has been the global sourcing of both active and inactive ingredients from emerging economies where costs are lower. Further, the manufacture of generic drugs or those coming off patent are also more likely to be outsourced to manufacturers in developing countries.

The long supply chain, with sourcing, manufacturing, packaging and distribution occurring in different locations globally, has increased the risks of contamination or substitution of alternative ingredients, as in the case of the 2008 heparin accident.

Sources of the counterfeiting problem are linked even with manufacturing outsourced: there are a number of unscrupulous manufacturers, many located in India, China and Southeast Asia, who will produce the counterfeit drugs and package them so they look authentic.

Strategic outsourcing addresses the decision whether to outsource and several related issues such as the risks associated with outsourcing, the expected results of outsourcing, and conditions for successful outsourcing. Outsourcing on the operational level addresses issues that are relevant after having made the outsourcing decision, such as how to manage the outsourcing relationship, how much to outsource, and which orders to outsource.

An outsourcing relationship can be more complex than a simple supplier-buyer relationship. The order process towards the contract manufacturers is complicated by the different connected decisions in time and the uncertainty of the available capacity from the contract manufacturer. Controlling a contract manufacturer operationally in the

same way as an internal manufacturing source leads to a nervous ordering behaviour with a lot of changes and a lot of panicky communication between the outsourcer and the contract manufacturer. It is essential to develop a more advanced order release mechanism that includes the various aspects of outsourcing, such as: capacity reservation, postponement, cancellation option, and the uncertain capacity allocation from the contract manufacturer.

The pharmaceutical industry is facing increasing costs of developing new drugs while R&D productivity has stalled. In an effort to counteract this, pharmaceutical companies have outsourced work to third parties both in their home markets and offshore in emerging markets like India and China (Kate Kuhrt, 2008).
Focusing on India, we can identify trends that are common at least within all the other countries among the so-called BRIC (Brazil, Russia, India and China) (Charles Conrad Uy, 2007).

What the multinationals now seek from India is the same combination of brainpower and cost savings that made the subcontinent a leader in software and computer services. Some Western companies are volunteering to share intellectual property rights on new discoveries and even share the profits. The rush east, where five PhD chemists can be had for the cost of one in the West, entails risks. At a time when Pfizer, AstraZeneca, and others are cutting U.S. R&D jobs by the thousands, the build-up in Asia is bound to set off alarms that America is sacrificing another key industry through radical outsourcing. But if the strategy works, it could save the drug industry billions of dollars, bring down the prices of new drugs, and accelerate breakthroughs.
Many Western executives say they're stunned at how quickly the Indian industry is achieving targets set by the joint ventures. Just a few decades ago, India was a outcast in the pharmaceutical business. New Delhi in the 1970s declared it would cease patents on Pharmaceuticals. Then thousand of generic drug-makers were born. The Indian executives argued they were providing a social service, selling antibiotics, say, for a fraction of what Western patent holders demanded. In the 1990s, Indian generics makers started selling AIDS cocktails in India and Africa at just $ l per dose.
Even Indian drug executives, however, realised the imitation business was a dead end.

Almost all of India's top pharmaceutical managers recognise the only way to jump-start a modern industry is through collaboration with Western drug companies. So in 2003, New Delhi reversed course and said it would protect the rights of foreign patent holders. The first collaborations involved fairly simple lab work, mainly to save on labour costs. The Indians wanted more responsibility.

Over time, the partnerships evolved into co-development arrangements.

For the Western partners, the first objective in these alliances is to cut costs. In the U.S., specialised research outsourcing firms will charge a drug company $250,000 and up for the full-time services of a PhD chemist. With an Indian partner, the same work can be done for roughly one-fifth the cost. But what Western companies long for, more than anything, is to replenish their drug development pipelines. It can cost as much as $100 million to develop a potential drug from a germ of an idea to the point where it is tested in people. After all that, the odds of any drug winning Food&Drug Administration approval are just 1 in 8. By conducting many experiments in low-cost Asia, the drug companies believe they can run more projects while keeping R&D budgets flat.

Western drug companies are giving Asian partners more responsibilities than they ever imagined. SuvenLife Sciences, an Indian start-up in Hyderabad, is co-developing drugs for brain diseases with Lilly. As part of the deal, Suven can work on its own drugs for Alzheimer's, obesity, and Parkinson's disease, provided they don't compete with jointly developed products. Early on, Lilly sought to impose restrictions on Suven's own research.

The benefits coming from the outsourcing of both drug manufacturing and research activities are relevant, but the pharmaceutical companies have to face a number of challenges.

# 3. THE ANSWER OF RFID TO THE PHARMACEUTICAL-INDUSTRY ISSUES

After presenting the main characteristics of the RFID technology and the main fields of application and after introducing the parties involved in the pharmaceutical supply chain and the key features and issues faced by this industry, now in the third section of this work the aim is to understand how the RFID technology can provide solutions inside the pharmaceutical supply chain.

In particular the chapter is structured to show first, how the RFID can perform for each of the problems presented in the previous chapter, then it presented a real case study reported by Kwock, Ting, Albert et al., and in the end, some guidelines to apply this technology inside the specific industry are provided.

## 3.1 Counterfeiting

As already said, companies are beginning to employ counterfeit-resistant technologies into packaging and labelling for a number of products, like: overt and covert features incorporated into the packaging and/or labelling of the product and chemical tags incorporated into the drug product itself (Goldhammer, 2006).

Overt features include holographic images, special stickers, inks of gradated colours, or threads in the container label, all of which can be used to verify that the container is authentic. Some of these approaches are similar to technologies used for document authentication.

Covert features include special inks, threads, or materials that are known only to the manufacturer and require special equipment (e.g., ultraviolet light source) to identify. Covert approaches also include the incorporation of small amounts of a chemical tag into the pharmaceutical preparation. Such chemicals can be part of the bulk formulation of active ingredient or incorporated into the gel capsule or film coating of the pill. The tag can be verified by chemical analysis by the company. Companies can also use the known analytical composition of the formulation for authentication purposes. For example, defined impurity profiles and/or amounts of different inactive ingredients as well as dissolution patterns can be tested to determine a drug's authenticity.

Counterfeit-resistant technologies serve 2 purposes, to:

- make more difficult and costly for counterfeiters to produce a convincing copy of a drug's packaging and/or labelling and
- provide companies a means for determining whether a questionable product is authentic or counterfeit.

These are important goals, and the Pharmaceutical Research and Manufacturers of America (PhRMA) thus supports the use of counterfeit-resistant technologies on appropriate drug products. PhRMA believes it is critical to the success of anti-counterfeiting strategies to erect as many hurdles as possible for the counterfeiters.

At the same time, it is important to recognise the significant limitations of counterfeit-resistant technologies.

- First, these technologies are merely resistant to counterfeiting; they are not counterfeit proof. Experts believe that such features must be changed at regular interval as counterfeiters will reliably duplicate them. In fact, it is the experience of PhRMA member companies that even elaborate approaches such as holograms eventually are counterfeited and that any such feature must be rotated every 12 to 18 months.
- Another limitation with counterfeit-resistant technologies is that they do not provide real-time verification of a drug's authenticity. Covert features and tags typically require specialised equipment or testing to authenticate and can and should be authenticated only by the manufacturer. These tests often cannot be performed on-site or require a manufacturer's representative to travel to the site. In addition, tests for tags may take up to several days to perform to accurately determine whether the drug is counterfeit. This may be problematic if a large amount of drug is of questionable authenticity as it would have to be withheld from commerce until the testing is completed.
- Although overt features theoretically can be used for real-time verification, they are easier to counterfeit than covert features and thus provide the least assurance of authenticity. It simply is not realistic to expect pharmacists or patients to routinely check, or even be aware of, the wide variety of overt features used on the thousands of different drug products available through pharmacies. This problem will be exacerbated by the need to rotate overt features on a regular basis.

- Finally, overt and covert technologies are rendered useless if a drug product is repackaged, a practice that is common in the industry and subject to only minimal regulation.

The US FDA advocates the adoption of track and trace technology and is promoting radio-frequency identification (RFID) technology that utilises an electronic product code (EPC) (Lybecker Kristina M., 2008).
Drugstores are also making an effort to eliminate vulnerabilities in the supply chain and enhance safety. In 2002, the drugstore chain Eckerd notified its wholesalers that the company would discontinue buying from them if they ever provided counterfeit drugs to Eckerd. Moreover, CVS Corporation recently announced that it will no longer purchase drugs from wholesalers that trade in the secondary market, which has been a point of entry for counterfeit drugs into the supply chain. Through strategic contracting and supply restrictions, pharmaceutical manufacturers are also reigning in their wholesalers and distributors. In late 2003, Johnson & Johnson decided that it would no longer sell its products to US wholesalers that buy J&J products from other sources.
Firm strategies extend beyond the traditional supply chain. According to a study conducted by Ernst & Young, drug-industry executives believe the Internet and mail-order operations will be the biggest source of counterfeit drugs over the next five years. As such, firms are turning to unconventional allies with whom to partner in the battle against counterfeits. For example, Pfizer Inc. and Microsoft Corp. announced a joint effort to reduce Internet sales of Viagra. In another Internet-related effort, Google Inc. and Yahoo Inc., which account for two-thirds of all Internet searches, both decided to limit search-related pharmaceutical advertising in the US to licensed US and Canadian pharmacies.

Even PhRMA member companies support the development of an electronic track-and-trace system (using RFID chips for package identification) that can track drug products in real time throughout the distribution system (from manufacturer to patient) and provide an electronic pedigree for the authenticity of distributed drug products. Electronic track-and-trace technology will be a key element in strengthening the closed pharmaceutical distribution system. Before such a system can be implemented,

however, complex technological, legal, regulatory, and financial issues need to be resolved by all interested stakeholders (Goldhammer, 2006).

The following schema outlines one approach for implementation:

1. The manufacturer places a machine-readable serial number on the packaging. The minimum data elements are the serial number and a pointer to the database in which the necessary information to identify the specific pharmaceutical is contained.
2. The first recipient of the packaged pharmaceutical electronically authenticates the serial number. A query to the database authenticates the number as being assigned to that particular package unit. The recipient's business information and transaction date can be electronically recorded in the database.
3. If a recipient of the pharmaceutical package does not authenticate the serial number according the above business practice, it will not be registered in the database. When the next recipient attempts to authenticate, the database query will respond with a message that the unit was not properly authenticated by the previous trading partner. Further distribution should cease until the cause for non-authentication is identified.
4. The serial number is closed out at the point of dispensing. Subsequent queries to the database for that particular serial number will result in a response that it is non-authentic.

There still remains a significant amount of work that needs to be done to move toward an electronic drug authentication system.

- Standards for mass serialisation must be finalised.
- A proper assessment of the read failure must be done as implementation of the technology as described above argues for as close to a 100% success rate in reads for serialised pharmaceuticals. Product that cannot be authenticated will be presumed counterfeit unless other systems are in place. In addition, there will be a tremendous amount of validation activities that will be required for start up of these systems within manufacturing environments, requiring a high degree of assurance that they will perform as intended. There have been some reports that the read rate for RFID-tagged biologicals, liquids, and metal packaging fall well short of this goal.

- Business and data exchange practices must be put into place. The supply chain must be ready to embrace the technology in a timely manner.
- In addition, the scope of products that will be mass serialised must be defined.
- Consequently, while electronic track-and-trace processes are developing throughout the distribution chain with the building out of the necessary information systems, patients will be benefiting from the real-time authentication of drug-packaging units at the dispensing site.

To move toward early adoption of electronic authentication, it is possible to propose the following steps:

1. All package units of targeted prescription medicines should contain a machine-readable serial number that includes the company identifier. The applicable package level to uniquely serialise includes the pallet, case, and item level.
2. An appropriate information technology infrastructure should be constructed that will allow the dispensing site and other trusted parties to query through a central data portal. Data will be routed to the distributed database, where information on the package unit in question is kept. The dispensing site will receive a real-time signal back that the identification number is authentic for the product in question.
3. Electronic authentication should focus initially on the end user dispensing site but is not intended to exclude other supply chain participants. Targeted pilots should also be undertaken by the pharmaceutical industry with the goal of furthering the development of electronic pedigrees.
4. Operating rules must be established regarding the point and time of authentication. Following dispensing of the package unit (or the opening of a container containing multiple dispensing amounts), steps should be taken to prevent the subsequent illegal use of that unit's serial number.
5. Following successful demonstration of the viability of dispensing site authentication, this technology can be added to other partners in the supply chain, adding another tool to ensure authentic pharmaceutical product flow from the manufacturer to the end dispensing site.

In addition to the actions above, the criminal penalties for counterfeiting prescription drug products must be significantly increased. For example, the current penalty under

the Federal Food, Drug, and Cosmetic Act does not reflect the serious public health risks associated with counterfeit drugs or serve as an adequate deterrent to prospective counterfeiters. PhRMA thus supports increasing the maximum criminal penalty for counterfeiting drug products from 3 to 20 years' imprisonment.

Finally, consumers also can play an important role in stopping counterfeits from entering the drug supply. They should purchase prescription drugs only from licensed US pharmacists. While a barrage of Internet pharmacy e-mails and Web sites promise low prices or access to certain drugs that are controlled substances, most of these are likely to be counterfeited. Internet pharmacies that display a verified Internet pharmacy practice sites (VIPPS) seal are licensed pharmacies through which FDA-approved medications can be purchased. These sites are identified by the VIPPS hyperlink seal displayed on the Web site.

FDA departments all over the world are interested in knowing the correct identification of medicinal product, materials used in the preparation of medicinal products, equipment and the areas used for manufacturing etc. They require and demand documentary evidence for all these parameters; however at present they are not insisting on a particular technology to facilitate this process. RFID can be a good candidate to address this problem (Manohar Potdar, 2006).

In the developing world counterfeit drugs are a major problem. Counterfeiters insert fakes at different points in the supply chain. They often sell directly to pharmacists, who think they're buying a discounted version of the real thing. According to the United Nations Office on Drugs and Crime, counterfeit drugs represent a $1.6 billion annual market in Africa and Asia alone. A handful of entrepreneurs are trying to make drug sales more reliable. Pharmasecure focuses on India. Aegate operates in Europe. And Sproxil, a mobile phone-based start-up in Boston, works in Nigeria. The founder decided to focus on Nigeria, because the Nigerian government is proactive about fighting counterfeit drugs, and Nigeria has a strong cell phone culture. Sproxil places scratch-off labels on bottles and blisters, instead of using RFID tags because of their high cost. When users scratch off the labels, they see a numerical code. They send that code, via text message, to a toll-free phone number, and immediately receive a text back

that indicates whether or not the drug is legit. The company makes money by selling the technology behind the scratch-offs to big pharmaceutical companies like Johnson & Johnson (Alberto Coustasse, 2010).

## 3.2 Secondary distributors

The grey market, the one made up by secondary wholesalers, is where the legitimate supply chain crumbles. An unauthorised source, using fraudulent pedigrees to sell tampered with or counterfeit drugs in legitimate channels of commerce, is where it becomes dangerous.

For instance, a pharmacy believes it has purchased an authentic product from a wholesaler and the patient in turn believes he/she has purchased an authentic product. In fact, the origin is unknown or disguised and the safety and efficacy is compromised.

Even in these situations RFID technology can play an important role, as is the case of the counterfeiting challenge [11].

The distributors may not have proper storage conditions: in fact for drugs that are sensitive to high temperatures and particular conditions can compromise the safety and effectiveness of the drug, we need to monitor the environmental conditions of the plant (Ann Marucheck, Noel Greis, 2011).

However assuring high-quality products requires that the manufacturing facility is monitored 24/7 and this monitoring requires the use of high end networking technology. Currently pharmaceutical plants capture this information using a number of scalar sensors that measure temperature, pressure, humidity etc. In some developing nations this sensed information is manually recorded by a supervisor in charge. This often results in data entry errors that need to be addressed, an alternative can be to capture this information and process it in real time to provide the kind of track and trace useful to monitor the plant. The solution can be use a Wireless Sensor Networks, that is a network composed of intelligent embedded nodes capable of communicating over wireless link with base station and other nodes. Researchers are working on WSN for environment monitoring and for security check (Potdar M., 2009).

The system comprising WSN network and RFID tags is shown in Fig. 8.

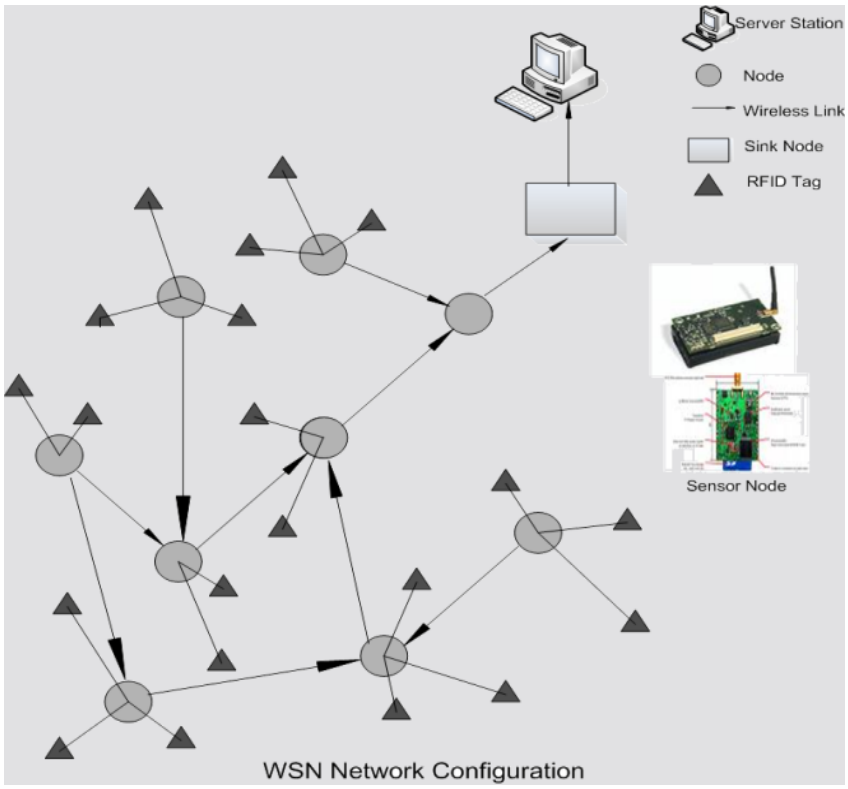


Figure 8: RFID-WSN Network Configuration ("Applications of Wireless Sensor Networks in Pharmaceutical Industry", Manohar Potdar, Atif Sharif,Vidyasagar Potdar, Elizabeth Chang, 2009)

## 3.3 Inventory and Warehousing Management

The pharmaceutical industry handles different types of material and hence identity and stock management is a very crucial and important activity. The materials handled are classified in different categories and their identification and movement tracking is very essential for the management of the pharmaceutical unit and also a critical requirement of the FDA in every country (Manohar Potdar, 2006). Tracking of all such material is a big task and a challenge that RFID technology can address. There are two main areas in inventory management and control where RFID can be useful:

- tracking entry and exit raw material and finished goods
- smart shelving and smart search.

*Entry and exit tracking.*

RFID technology can have direct and useful applications in tracking the entry and exit of goods in a warehouse. All material entering the pharmaceutical manufacturing unit must be identified by the supplier name, manufacturer name, product name, batch numbers, quantity, dates of manufacturing and expiry etc. Other than that, there is a list

of certified vendors from which a particular material must be purchased. If each arriving container has a RFID tag to identify the suppliers or manufacturers, it would facilitate easier track and trace, at the same time it would help to certify that the material has arrived from the approved vendor. However, if this check fails then the material can be quarantined for further investigation.

This test can be done at the entry site of the materials department or warehouse. This would prevent accidental use of the wrong category of materials, since FDA insist on use of tested and approved materials in manufacturing.

RFID tags can help to validate the manufacturing and maintain quality control and quality assurance by documenting that only approved materials are being used.

If RFID tags are fixed on transportable finished goods packs, it would facilitate the maintenance of automatic track and trace of all the materials leaving the manufacturing unit, which would further help in knowing and maintaining correct stock of all the finished product goods.

*Smart Shelf and Smart Search.*

Smart shelves are shelves that know what they carry, which means, they can be searched from a distant location and can offer the precise location of product or pallet. The capability to search the pallet location within the warehouse would save time and reduce the manpower associated with such administrative tasks, as well as facilitate decision-making. RFID technology can offer smart shelving and searching solutions. To do this all shelves in a warehouse should be first uniquely identified; this can be done using RFID tags. Each unique shelf location could then be used to associate it with a pallet. Hence, whenever a new consignment arrives at the warehouse, the RFID system can direct the consignment to the most appropriate location within the warehouse. Since the RFID system is capable to keep track of all the empty shelf space in the warehouse, the whole process can be automated. The whole warehouse can thus be operated from a remote location. The concept of smart can be further be extended to facilitate manual lookup, in large warehouse, it would be extremely beneficial if the exact location is highlighted by a LED or a bulb (pick-to-light system). Hence when a pallet is searched from a computing device the relevant LED would light up to exactly show the location

of the desired pallet. This would facilitate the warehouse operator to load and unload pallets then they enter or exit the warehouse.

## 3.4 Integrating the supply chain components

For the aim of integrating the supply chain components we need to gather a huge quantity of information inside the industry, because we need to take decisions about how to design our distribution channel and to set the level of inventory and the production capacity used by each plant.

The information, that is necessary, is about the actual flow of products between each production site and the level of inventory present at the manufacturers in each moment during a period of time.

Product ID authentication is enabled by assigning a globally unique serial number to each drug product, which distinguishes it from every other item of the same pharmaceutical product. Encoding the package of a pharmaceutical item with a unique identifier is known as serialisation. The serial number can be used to track and authenticate the product as the product moves through the supply chain, and so can provide the information required for designing and integrating our supply chain (S.K. Kwok, 2010).

The authentication service provides a quick and easy method for wholesalers, pharmacies, and other dispensing end points to verify that the product serial number is authentic, that it originated from the pharmaceutical manufacturer, and that it is in a valid state (presumed to be safe) (Deus Lucia 2006).

To enable a drug product for product ID authentication, a pharmaceutical company serialises each individual item, maintains a database of information about each item, and makes a service available for authorised downstream trading partners to query that database.

Serial numbers can be applied to product packaging using RFID tags. As reported in the first chapter, EPCglobal has developed the electronic product code (EPC), a numbering format for the mass serialisation of items.

The pharmaceutical company maintains a database of information about each serialised product that is enabled for authentication. The information can be used by downstream trading partners to establish that serial number was assigned by the pharmaceutical

company and that associated product information matches the physical product. The pharmaceutical company can make other product information available, including physical anti-counterfeiting measures, product status (such as recalled, stolen, and expired), and whether the product was in fact shipped.

To allow downstream recipients of products to authenticate them, the pharmaceutical company makes a service available on the Internet such that recipients can query the database with serial numbers read from product packages. Results are returned to the downstream recipient in real time. The pharmaceutical company may make the authentication service available to these recipients or it may rely on third-party authentication services.

An authentication service is typically a Web site that allows users to enter serial numbers and view the results of the query. Items may be authenticated at any point or at multiple points in the supply chain. A wholesaler may authenticate an entire pallet of items, and then a pharmacy may authenticate the same items individually when they are delivered. RFID technology accelerates the process when it is configured to collect and submit serial numbers for the query.

The results of item authentication may notify pharmacists of recalled products or other safety concerns earlier, more reliably, and more consistently than other methods of communication. The authentication service may also provide guidance regarding physical anti-tampering measures and other safety features of the item packaging.

The use of a pedigree to secure the distribution channel was introduced by state legislation, and to date, more than 10 US states have adopted pedigree legislation. As more and more states have adopted pedigree laws to secure drug distribution, technologies and standards for enabling secure electronic pedigrees have emerged in the marketplace.

An electronic pedigree is a document that describes one or more pharmaceutical items and records the details of each transaction in which ownership of the items is transferred.

Figure 9: It shows the RFID label applied to a drug package (“A counterfeit network analyzer based on RFID and EPC”, S.K. Kwok, S.L. Ting, Albert H.C. Tsang and C.F. Cheung, 2010).

The pedigree records detailed information for each change-of-ownership transaction and the companies involved, including the business addresses, shipping addresses,

transaction identifier (such as purchase order or invoice number), transaction date, and quantity of items in the transaction. Finally, the pedigree includes a signature from the company certifying the information that is recorded on the pedigree about a transaction.
In order to secure the transactions of its drugs in the distribution channel, the manufacturer initiates the electronic pedigree record and makes information describing the drug product and the sale transaction available. It then certifies the pedigree with a digital signature. When the drug moves through the supply chain, the pedigree is electronically transmitted to the receiving company. The pedigree system for the receiving company electronically authenticates the pedigree to verify the integrity of the signed transaction. For each subsequent sale in the supply chain, each company adds the new transaction details and certifies the pedigree with a digital signature and passes the pedigree to the next supply chain partner to be verified against the shipment. When implemented using commercially available technology and standards, the electronic pedigree offers security that functions at the scale and speed required by pharmaceutical supply chains.

Figure 10: RFID-based Pharmaceutical Process ("RFID Application Framework for Pharmaceutical Supply Chain", Dianmin Vue, Xiaodan Wu, Junbo Bai, 2008).

RFID can play its tremendous advantages to help pharmaceutical supply chain to ensure not only its security but even to increase efficiency.
RFID-based pharmaceutical manufacturing process, as is shown in Figure 10, is made up by different stages (Dianmin Yue, 2008):

- when the pharmaceutical enterprise purchases raw materials, it requires suppliers tag raw materials in order to guarantee the safety of drugs and write the tag. The EPC information includes the supplier name, raw materials names, quantity, unit price, and other information. Manufacturer tests their warehouse, updates inventory records when materials check in. While the materials check out, the same task needs to be done;
- during the manufacturing, because most of the materials are processing in pipes, the security is already guaranteed, so we don't tag them temporarily. We only scan and mark the materials when they enter into the pipes, control time efficiency, and package the products when they leave the pipes;

- packaging stage, first of all, manufacturer assigns a unique EPC number to each product. Packaging supplier writes the tags assigned by manufacturer and embeds the tag in empty packaging materials. The information includes drug name, number, production date, validity, effectiveness, etc. After the primary packaging of drugs, the product then proceed to level packaging, and increased information in order to track the drugs during shipping.

In the process of tagging, with RFID technology and EPC, the main purpose is to make the information shared among pharmaceutical manufacturers, wholesalers, retail and hospital, they can track the drugs, in order to enhance the visibility.
From the above analysis and design of view, RFID can be applied to the whole pharmaceutical processes: purchasing, manufacturing, packaging and delivering. During the process of RFID application, it can improve the efficiency of the pharmaceutical process, enhance the transparency of the pharmaceutical process to ensure drugs security in the manufacturing and transportation.

If RFID technology is widely used in every stage in pharmaceutical supply chain including manufacturing, transportation, sales, usage and recall so on, pharmaceutical companies on the supply chain will share the information stored on RFID tags and can timely know the use of drugs, and then strengthen the efficiency of the whole system.

A real example can help clarify these aspects.
Today pharmaceutical companies are moving forward with these more comprehensive approaches and securing real drugs to protect patients.
In January 2006, Pfizer began applying serialised RFID tags to all Viagra products sold in the United States. Pharmacies and wholesalers authenticate the EPC serial number on each bottle of Viagra and confirm that it is valid and was issued by Pfizer for that drug. More than 100.000 Viagra serial numbers have been authenticated by leading wholesalers and pharmacies, as well as smaller companies. Customers authenticating Viagra employ both high-velocity scanning techniques to check the product as it passes through normal warehouse operations and single serial number checks at pharmacies.

In addition to providing important consumer and brand protection, the program opens an efficient channel for managing communication of broad product issues that have previously been handled by thousands of e-mail and fax alerts.

In order to take advantage of the extra layer of security, pharmacies will need to invest in RFID readers, which pick up the radio transmission from the RFID chip. The readers then communicate with Pfizer servers to verify the product code.

Pfizer said it has invested several million dollars on the RFID project for Viagra. The application is not yet capable of tracking and tracing the pills throughout the supply chain, a capability that would require additional investments. Pfizer is exploring the possibility of implementing track and trace support in the future.

Privacy advocates have cited concerns about the use of RFID in the supply chain for fear that the chips can track consumers' buying habits or transmit other personal information. Pfizer said that their chips are unlikely to travel home with consumers, though. Pharmacists typically dispense Viagra pills in quantities smaller than the amount that comes in a bottle from Pfizer, so it would be rare for a customer to end up with a bottle of Viagra with the RFID chip.

Microchips are installed in drug-bearing pallets so shipments can be traced across the country. In some cases, even the individual bottles are tagged. Bottle tagging is more expensive, but it means that individual patients, or the thieves who stole their bottles, can be tracked.

In 2006, there have been significant developments in regards to RFID tagging of prescription drugs.

For Pfizer the decisions to move to RFID on these specific items were based on the popularity of these specific products, both in the mainstream and grey markets. All are amongst the leading counterfeited and diverted prescription drugs today (Deus Lucia 2006).

## 3.5 Information flows

In pharmaceutical manufacturing operations many activities, areas, materials and documents are required to be handled by several people. Some of these are critical and confidential and hence not everyone is allowed to access them. This is required to maintain a level of secrecy and operational safety. One approach to address this issue is providing selective access. RFID technology may be used here to restrict access to authorised resources. There are different areas in the pharmaceutical industry, where RFID can be used for access control (Manohar Potdar, 2006).

All pharmaceutical processes are required to be validated before they are used to manufacture a specific product. This shows that documentation plays a very important role in the pharmaceutical industry. Some examples of confidential documents include reports such as product development data, product stability data, technical audit, report of FDA, product recall and market complaints, etc. Document like these and several others are required to be handles with secrecy and confidentiality. These documents should be protected from being misused and intentionally corrupted. All critical documents must be clearly identifiable as original and genuine. Such documents have a separate physical area having restricted physical entry and selective access. RFID can be used for access control in two ways: to restrict human access high security area like this and to prevent movement of such documents in and out from these premises.

All critical and confidential documents could be printed on RFID tagged papers. RFID tagged paper is similar to a normal paper, but has a barcode and a RFID chip underneath. It can be printed from RFID-enable printer. Hence using RFID can address the security issue with physical movement of confidential documents.

As above mentioned, integration of RFID and EPC holds the promise of unprecedented supply chain visibility, so as to facilitate the information transmission among the supply chain parties. With correct implementation of such system in place, accurate and reliable supply chain information can be visualised for improving the whole system. It is expected that such integration is a promising approach to address the problems in pharmaceutical supply chain, especially the issue of insufficient information transmission (Ting S.L., 2010).

Each medicinal product is attached an EPC tag for identification purpose, for example a 96-bit EPC tag has enough capacity for most applications. So the company can store not only information about the serial numbers of each product, but even the production date, manufacture information and shipment data. With the help of the automatic capturing capability of RFID, the product information can be updated from point to point, and users can even simply visualise particular product information by enquiring the unique identification code. Thus all the parties, from the manufacturers to the end customers, can be benefited by the implementation of this system (Alberto Coustasse, 2010).

The self-developed EPC network supports more effective communication amongst the supply chain participants, enabling visualisation of hidden supply chain information. Through the adoption of RFID technology and the EPC standard, companies can view the life-cycle transactions of products on a user-friendly interface. All such information is stored in the centralised databases, closing the decision-making gaps between supply chain participants (S.K. Kwok, 2010).

In particular important information about the level of inventories at the drugstores can be provided, in order to simplify the order information flow.

Figure 11: The safe and secure supply chain model secures model secures both physical items and transaction records ("Technological Roles in Combating Drug Diversion and Counterfeiting" Lucia Deus, Journal of Pharmacy Practice, 2006).

## 3.6 Traceability and recalls

Large global recalls associated with recent product safety events, for example the Chinese melamine-adulterated milk contamination in 2008, the adulterated Heparin in 2008 and the Toyota recall of 2011, have made the development of tools and technologies for traceability through the supply chain a critical issue in risk control. For consumer products, traceability studies have addressed access to the supplier network for more immediate recall of products (Ann Marucheck, 2011).

However, with respect to medical products, such as pharmaceuticals and medical devices, the ability to track and trace is critical to detecting if a product is counterfeit while also deterring intentional contamination, adulteration and diversion of legal products. This is an area where technology originally developed for tracking inventory and assets in the supply chain has proven to be very useful: an electronic pedigree which can provide information about the route of a product at the package level through the supply chain from manufacture to final use. Due to the special challenges in ensuring the safety of the pharmaceutical supply chain, recent legislation is requiring that all pharmaceuticals sold have an electronic pedigree or some unique product identification. In addition, to providing authentication of the product, these identifiers would provide critical information in the event of a recall. The ultimate goal is to have complete transparency of documents, information, and goods across borders. RFIDs are already considered a supply chain technology, but many consider them an inventory tracking tool that is used to address inaccurate inventory records. The use of RFID for tracking and tracing is still in its infancy, but it has great potential as the price of the tags declines and more companies adopt the technology.

In the area of recall management, there are several unresolved questions related to risk discovery. They include identifying a product safety problem and mitigating the risk from a recall.

One of the critical issues in identifying safety problems is the sharing of timely and accurate reporting of information regarding product reliability and malfunctions. Many companies lack the type of timely and complete information required to confidently make the decision to recall, however a delay in issuing a recall can lead to higher losses and risks more damage to the firm's reputation. Companies may be wary of sharing information that they view as proprietary and possibly damaging. The bottleneck may

lie in having enough data and information to use these sophisticated information technologies in managing recalls. Operations management research, that addresses information sharing in collaborative supplier relationships, may provide insights to how product safety information can be collaboratively shared within an industry.

A second question is how to best mitigate the risks and losses associated with a recall. Communication is a key element of an effective recall process. Speed of response is the most crucial variable to control the effects of risk.

Product recalls and product counterfeiting are public safety issues. With improved visibility of supply chain information, companies can respond to public safety incidents more promptly and efficiently in identifying the products that need to be recalled and tracking the counterfeits. The proposed system effectively tracks products throughout the global supply networks, sharing product data for detection of counterfeited drugs in the supply chain.

## 3.7 Outsourcing trend

Another area that offers challenges for further research is the management of supply chain relationships. Many companies have outsourced manufacturing to lower cost countries around the world, because of the concerns about cost reduction, and so this phenomenon combined with the additional complexity of the supply chain will continue to lead to safety problems.

A question is how to coordinate and monitor the behaviour of suppliers with respect to product safety. Information technologies are increasingly being explored as tools for better coordination and monitoring of the manufacturing process to avoid quality and safety problems, in particular RFID technology. Companies must invest time and effort in developing not only standards and principles of safety for their suppliers, but must also invest in education and training to build the skills and abilities within the supplier network to assure product safety.

Another question is how to effectively educate suppliers. Even the FDA is taking a more collaborative approach and stressing education and training in its practices with foreign countries. Included in FDA's budgets for fiscal year 2010 were specific items designed to improve product quality and safety in the medical device industry. For example, it proposed to provide onsite training to foreign regulators on medical device

safety and quality. Also, it proposed to develop supplier relationships that promote and provide incentives for safety with suppliers, including the implementation of cost-sharing contracts for recalls.

## 3.8 An example of RFID application in the pharmaceutical industry

A significant example is provided by Kwock, Ting, Albert et al. in "A counterfeit network analyser based on RFID and EPC", in which they present the example of a Chinese pharmaceutical company Harmonic that decided to apply the counterfeit network analyser inside its supply chain.

A counterfeit network analyser (CNA) integrates the automatic data capture technology (RFID), information sharing network (EPC network), higher security measure, and social network analysis concept. It is designed to perform three functions that include automatic product identification, encryption and decryption, and intelligent detection of the counterfeit source. The automatic product identification function refers to continuous monitoring of the condition of pedigree information. Through the encryption and decryption function, the information shared and uploaded in the EPC network can be enhanced to a higher level of security. On the other hand, the intelligent counterfeit-source detector is used to discover a potential counterfeiter within the authorised supply chain by computing the emission level of the counterfeits.

Harmonic Health Pharmaceutical Co. develops health foods and beauty products extracted and purified from pure Chinese medicines. The company's health food series have been selling in the market since 1999, and the company has been a pioneer in the production of Chinese medicine capsule pills. Over the years, these pills established a good reputation in Hong Kong, but this has also attracted the attention of counterfeiters, causing subsequent loss of business and damage to the goodwill of the company. Harmonic has modified the packaging design of these products four times in the last two years with the aim of differentiating its genuine products from the fakes.

Owing to the fact that the original packages were found to be counterfeited very quickly, the company suffered from potential business risk which adversely affects the business operations of the company. Moreover, Harmonic needs to distribute the products around the world and many activities would take place at each intermediate

point in the supply chain. To avoid any counterfeiting behaviour existing in these intermediate points, the company requires the supply chain party at each immediate point to manually record the information in Harmonic's single standalone database via a web-based system. However, such approaches have suffered from human error and many parties are not willing to update the data in the system. Owing to the potential drug hazard (as the drug can be changed or counterfeited easily), the lack of visibility of the product flow, and the expensive repackage design, Harmonic decided to apply the CNA.

Figure 12: Conceptual framework of the information flows between the proposed supply chain network and stakeholders ("A counterfeit network analyzer based on RFID and EPC", S.K. Kwok, S.L. Ting, Albert H.C. Tsang and C.F. Cheung, 2010).

In order to set up an RFID environment, Harmonic and its authorised parties in the distribution channel are required to adopt the following prerequisites:

- Harmonic has to apply a range of universal unique EPCs from the industry-driven standard and encode the EPC information into each product's RFID tag, hence encoding the product information in each RFID tag that is compatible with the EPC standard.
- Companies in the supply chain need to register with the EPC network and install an RFID reader to capture the RFID signals.
- A data warehouse is established in each supply chain party for storing the transaction data, in which it can be accomplished by setting up a database system.
- Harmonic needs to define the product flow in the supply chain, by considering what information should be captured and who can access the information.

The tag was placed inside the package to prevent people from removing the tag (see figure at page 60). Furthermore, the box was sealed with a security label sticker (with company name) to protect it from being transferred by unauthorised parties. All these security measures helped to minimise the problem of unauthorised tag removal.

The RFID reader was able to simultaneously record 500 tags with an average reading time of a second. It can correctly read tags with an accuracy of 100 percentage when there are less than 100 tags scanned in one time. Therefore, it is designed to enable 50 packages to be put into a big box when they are shipped and delivered to other parties. The results of the tests indicate that there is about a 1 percentage error rate due to the reading conflict, and two readings were required to detect all the tags correctly.

Each healthcare product is first tagged by RFID at the manufacturing site, thereby providing detailed information on the product. Every party in the supply chain network (i.e. from manufacturer to retailer) is equipped with RFID readers to register the point-to-point transactions of the products.

Compared with the current manual operation in the collection of supply chain information, RFID demonstrates its automatic feature for data acquisition, which enables an end-to-end supply chain visibility with high accuracy. With the high readability and accuracy of the RFID, the unwillingness or incorrect human input can be greatly reduced when CNA is adopted. As a result, Harmonic is able to search and retrieve the product's supply chain transactions and the history of a specific product movement from the EPC network.

The CNA not only enhances the effectiveness of product authentication, but also estimates the possibility of a counterfeit source based on the use of social network analysis. It enables users to monitor and detect the counterfeit source distribution via a standard browser. Aggregation of all problematic ePedigree provides important information for Harmonic to estimate which supply chain party is problematic. The detection is accomplished by the social network analysis, a graphical representation. The likelihood of a party being a counterfeit source is colour coded for ease of interpretation. A node with a lower possibility is denoted in light yellow colour and the colour changes gradually such that a node with the highest possibility is shown in dark red colour. Based on the graphical result, Harmonic can identify the questionable parties and scrutinise such intermediate problem areas. Mainly, the system fully captures the product flow data across all the intermediate points.

Owing to the complexity of the Harmonic supply chain network, it is difficult to monitor where the counterfeit originates. Consequently, these counterfeit drugs not only threat public health but also lead a loss of sales and reputation, as customers may feel less confident in purchasing the products. To cope with these problems, the supply chain information visibility featured in CNA has helped Harmonic to discover the counterfeiting some as well as improving the company image by selling genuine drugs.

## 3.9 Guidelines for applying RFID in the pharmaceutical industry

Because of the generally higher per unit values of the products that they make and distribute, pharmaceutical manufacturers and distributors have the luxury of not being as cost-centric about RFID technology (particularly tag costs) as consumer product companies. While tag costs are certainly critical, they should not be the singular focus of companies that wish to achieve the maximum Return On Investment (ROI) from RFID technology (Vivek Bapat, 2005).

Additionally, pharmaceutical companies cannot look at RFID from a purely traditional ROI perspective, but have to consider the potential economic consequences of not applying RFID technology to a single drug whose credibility and sales are compromised due to widespread counterfeiting.

There will be a minimal ROI in the near-term, but in the long term, RFID is the right approach for product authentication and creation of an electronic pedigree through the supply chain. There are significant benefits in pharmaceutical industry in identifying product from the point of manufacture to the retail pharmacy and in sharing and make the information visible up and down the supply chain.

Despite advances with RFID, several issues need to be resolved before widespread adoption is possible. Without established standards, many companies are reluctant to invest in the technology. Furthermore, the implementation of RFID technology affects many different areas of a business and can become quite costly to execute.

A critical piece to the puzzle is the development of standards around data exchange, numbering schemes, and tag frequencies.

Additionally, there is the cost factor. Although the price of tags has come down over the past year, implementation of the technology as a whole remains expensive (30-35 cents a tag per unit) [11].

It takes a cross-functional effort to implement RFID technology and a lot of dedicated resources because it isn't an off-the-shelf technology. Implementing the technology involves many different functions within a pharmaceutical organisation because it is such a highly regulated business.

While the industry sees the need to implement anti-counterfeiting technologies, many companies are also waiting for anti-counterfeit products to be commercialised by others before implementing the solutions for their drug products.

For years, manufacturers have invested in ways to link production with supply chain information to not only optimise inventory, but also to improve production efficiency, flexibility, and responsiveness. For these manufacturers, a combination of RFID investments can quickly and cost-effectively deliver functionality (Vivek Bapat, 2005).
For optimal RFID success, efforts to improve inventory visibility across the supply chain should be closely tied to a company's control systems and execution processes driving production.
By applying RFID technology incrementally across the plant floor, manufacturers can seamlessly integrate the new information captured by RFID, without disruption, into existing, proven, industrially hardened control, visualisation and information infrastructure, reducing the need for purchasing new infrastructure or investing in expensive, time-consuming, and unproven IT integration projects. Existing manufacturing execution and information systems can then be updated to deliver robust and reliable real-time information flow to drive manufacturing execution in tune with the RFID-enabled supply chain.
Manufacturers are increasingly learning the importance of designing and integrating RFID information and solving connectivity issues related to plant floor and warehousing execution so that the new information is integrated into the plant floor reliably and through industrially hardened conduits.
Some guidelines about how to apply RFID inside the supply chain follow. These guidelines can be easily used and extended at the case of pharmaceutical industry.
*1. Business Case Justification and ROI Analysis*
This first step includes helping a manufacturer develop a complete ROI analysis to support budgetary needs and investment outlays across the entire supply chain. The ROI analysis will address numerous business issues:

- Where will the production and service disruption be minimal, but the returns the fastest?

- What incremental investments will be needed as part of a long-term strategy, and during what time frame?
- By conducting simulations and pilot programs, manufacturers can better understand the ROI of their potential RFID investment.

*2. Design and Architecture*

In this step, manufacturers can select tags and readers that are most suited to their environments, provide piloting assistance related to RFID laboratories, set up mobile labs for testing in the customers' environments, and arrange lab tours at existing internal or customer sites. Additionally, manufacturers can design an integration strategy with their existing bar-code implementations and a methodology to integrate their RFID information into their ERP systems, including providing case-to-pallet validation at end-of-line operations.

Another important aspect of this step involves helping manufacturers reliably and cost-effectively synchronise their RFID information with their control systems; help them design process and automation capabilities to facilitate item-level tracking and tracing functionality.

*3. Software and Systems Integration*

In this step, manufacturers can comprehensively integrate their RFID implementations into mainstream manufacturing and warehousing operation, from the ERP level to the control level. This step also includes integration with middleware and integration with local database management systems, ERP systems and control systems.

*4. Maintenance and Support*

An RFID project doesn't stop after it is implemented. There is an ongoing process of maintenance and support to ensure that all aspects of the RFID implementation are continuously monitored and supported at an engineering level, as well as from an information service perspective.

## The RFID Adoption Cycle

Although companies can gain significant business value by deploying RFID technology, a supplier can't simply slap a smart label - one with an RFID tag embedded in it - on cases, stack the cases randomly on a pallet, and expect to accurately read every tag.

Suppliers must resolve several production-related issues before applying RFID for tagging product. For example, products with high liquid content or containing metal (in the product or its packaging) require special consideration since liquids and metals can distort or impede RFID radio waves. Potential solutions might include using a specific type of tag, placing the tag in a precise location on the case, or arranging the cases in a special configuration on a pallet. Many companies are learning through trial and error.

According to several industry analyst groups, the RFID adoption cycle for most manufacturers typically progresses from pallet-level tagging to tagging individual products.

Leading manufacturers are quickly investigating and adopting RFID initiatives from both short-term and long-term strategic perspectives. This is being accomplished in a two-phased approach, summarised as follows:

*Phase I: Tag Application*

This phase predominantly consists of closed-loop piloting activity that is internally managed through pilot teams consisting of engineering, warehousing, IT, and plant managers. Phase I activity examples include devising solutions that trace products at the pallet level and matching the information to a production order. For manufacturers, the main issues in this phase revolve around validating tags, checking errors, and comparing the reliability standards of RFID to those of bar code technology.

*Phase II: RFID Deployed as an Integral Part of Operations and to Gain Strategic Advantage*

This phase includes tactical and execution plans surrounding increasing levels of integration of RFID deployment into mainstream business operations. As part of this phase, manufacturers ask key questions such as:

- How far downstream into manufacturing and out into the supply chain should RFID be implemented?

- How far upstream and at what level of granularity and into the production process should RFID be implemented?
- Which types of standards, software, and integration should be deployed?

For pharmaceutical manufacturers seeking to better manage inventory and more rapidly conduct recalls and reduce counterfeiting, theft, and shrinkage, RFID technology is clearly superior to any other competing alternative.

Companies in this industry would be wise to think about the potential benefits of RFID far beyond just a ROI equation; the potential consequences of not applying this technology are too large. Instead, companies should look to and learn from the RFID success examples provided by others within their industry, work incrementally with the right strategic partners to add RFID technology to their own operations, and begin to enjoy the innumerable benefits which RFID technology promises.

## 3.10 Discussion

The main problems faced by the pharmaceutical supply chain and presented previously in this work, can be solved and addressed properly by using and integrating RFID with the technology already in use inside the industry.

For what concerns the main and more dangerous problem, that is counterfeiting, the traditional overt and covert solutions used in order to avoid it are not able to totally protect medicines from people that try to break into the supply chain in order to make drugs become inactive or incorrect, or sub/super-potent. Indeed these solutions do not give any proof of the counterfeit identification, but they try to be resistant to counterfeiters; instead RFID is able to make more difficult to enter in the supply chain, by storing information about each party involved in the industry, and by integrating all the members in a unique information system. Each member of the industry will store its information in the tag and check if the previous stored data are reliable or not.
This technology is able even to identify in which part there is a slack or a break, so which party is the counterfeiter.

The recall process is linked to counterfeiting; when a batch of product is identified as not legit so it is needed to recall it before it reaches the market by causing possible damages to the population. First of all, there is the need to identify where the batch is, and so the track and trace system may be really useful for this purpose.

To best mitigate the risks and losses associated with a recall, communication is a key element that helps to improve the visibility and to respond to public safety issues more rapidly.

RFID can control the storage condition of the products, in particular for those that require certain level of humidity or temperature to be preserved. So the integration of RFID system inside a Wireless Sensor Network may be capable to monitor the plants, so that a lower number of employees may be occupied by automating this control.

The efficiency of the industry may improve by using RFID to manage the inventory system, so that it is possible to track and trace the products that enter inside the plant and those who exit from it. The system can provide accurate knowledge of the current

level of inventory, in order to avoid the stock out of the material, that is a critical point of success for this trade.

RFID may be even used for managing the information flows not only about the transaction between the trade partners, but even secret information about product development data, technical audit, report of FDA, product recall in order to prevent movement of such documents in and out without permission.

The advantage of this technology is the supply chain visibility provided that assures more effective communication and collaboration among the involved parties. Particularly important is the possibility to share information about the level of inventories at each stage so that it will be possible to make the ordering flow easier. This capacity is especially important in this sector because of the outsourcing trend that requires manufacturers to manage supply chain relationship in a proactive way by avoiding safety and quality issues.

The global advantages provided by this technology are:

- lower costs due to the avoidance of the loss of image and loss of money for the recall of product identified as counterfeited more downstream;
- the capacity to identify the point of the supply chain where the counterfeiter breaks inside it;
- the origin and authenticity of the product is secured;
- higher visibility of the supply chain and of all the component behaviour;
- higher level of quality for the product thanks to the monitoring 24/7 by the WSN;
- the improved communication among participants;
- higher level of efficiency in managing the inventory at each step of the supply chain;
- significantly reduce cost and time required for physical inventory: the time it takes to do physical inventory is reduced by 90% from several man-days to a fraction of a day;
- management could reduce monthly inventory level;
- the resulting RFID-based inventory will be more accurate;

- the possibility to eliminate stock outs of product categories with high level of inventory turnover,
- leading to improved revenue and customer satisfaction;
- provide vendors with real-time visibility of inventory, product is automatically registered as it passes through RFID-equipped dock doors, providing location information;
- a strong link is created between package, unit and pallets level;
- RFID tagging process does not affect the supply chain throughput.

Although RFID has demonstrated considerable benefits in counterfeit prevention, there are numerous challenges in the global adoption of such technology.
Implementation of an RFID system is costly, time-consuming and difficult. The problems encountered in a typical case study as well as its solutions are explained and discussed below:

1. Cost issue. Cost is the most remarkable challenge in adopting the RFID technology. The tag cost and customization cost demands companies to invest enormously in building the network. Thus, it is learnt that effective containment of costs is critical to successful RFID implementations. Phased implementation is one of the suggested solutions that will benefit the company within the shortest period of time. Furthermore, leveraging experience gained from the pilot implementation would help companies to replicate successes and avoid danger in full-scale roll out of the solution and minimize wasted investment.

   In the table below the main costs for the implementation of the RFID system inside Harmonic company (case study page 69), are reported:

| Implementation cost | |
|---|---|
| RFID hardware set up cost (1 RFID printer + 7 EPC compliant, multi-protocol reader ) | 15200 € |
| Software customisation cost | 10500 € |
| Monthly running cost | |
| RFID tags (€0,20 * 2,000 products) | 400 € |
| Maintenance cost | 314 € |

2. Standardization issue. The penetration power of radio frequency energy depends on the transmitter power of the reader and duty cycle. These are regulated in many countries around the world. For example, a reader might fail to communicate with the tag attached to a product because it is designed to operate at different frequencies. This type of detection problem discourages many supply chain parties from adopting the RFID technology because they are uncertain about the effectiveness of the system they invested in. In the absence of a globally unified RFID frequency band, company should standardize the operational bands of the RFID system components used by the collaborating parties.
3. People and organizational resistance. People will typically reject a new approach when the existing process has to be significantly changed.
4. ePedigree defining issue. With the help of RFID and EPC, the ePedigree can be formed according to the captured information. Numerous issues remain open question and require further study, such as future transaction volumes, information storage (how long will the organization be required to store the drug pedigrees?), reliability and certification (when will the pedigree be required to register the information once the product is shipped or is at other stages?), etc.
5. RFID Difficult Materials. The materials that make up the medications are mainly metal and liquid; both materials can highly affect the way radio waves behave when you are intending to identify via RFID tags in close proximity to them. To resolve this problem, it can be used a UHF EPC Global Gen2, but this may increase the cost of the implementation.
6. Manufacturing Process Speed. Packaging lines for pharmaceutical products tend to operate at high speeds capable of producing hundreds of units per minute. So it is needed to verify the premise that the use of this technology should not affect manufacturing processes speed.
7. Reading and Writing Process. Reading and writing variable data onto individually RFID tagged products moving at high speed and which additionally are packaged in metallic blister packs is extremely complex. The use of UHF RFID bulk encoding technology and the state of the art of software capable of writing via RFID to multiple units per pack at high speeds provided, this challenge can be addressed successfully.

The healthcare world is a large complex network of legislation, corporations, and fast growing technology.

In healthcare RFID is growing very rapidly and is projected to grow further into a $2.1 billion industry by 2016.

With the FDA's interest in e-pedigrees and the State of California's new requirement of individual serial numbers for each pharmaceutical unit, the supply chains of the past are being changed forever.

The results of the Viagra pilot, conducted by Pfizer, have further added to the success stories of RFID used in the itemized world of pharmaceuticals.

The requirements of the pharmaceutical industry are very different from those of any other industry and this is reflected in its rapid adoption of RFID.

Even the FDA recommended that all item level prescribed drugs supplied into the US market be RFID tagged within two years.

This is not going to happen on time, partly because of the thoroughness applied in investigating whether HF or UHF is the best solution and work on standards and what security and data handling should be used in the computer systems.

However, a good start has been made. The world's largest drug company Pfizer, which had earlier led the way in using 2D barcodes on drugs, has once again led the way with item level RFID, tagging all packages of Viagra from December 2005.

Viagra and Trizivir are already tagged in the US. Trizivir an HIV medicine, is one of the 32 drugs listed as most susceptible to counterfeiting and diversion.

As each bottle of Viagra moves down the packaging line, a label with an integrated passive high-frequency (13.56 MHz) tag is applied.

An RFID interrogator then encodes an EPC to each label, after which a second interrogator verifies the tag has been successfully encoded and can be read.

The interrogator also reads the unique ID number stored on the tag's chip by the chip's manufacturer, enabling Pfizer to record both the chip ID and the item's EPC in a database.

Pharmacists and wholesalers will use the tags to authenticate the drug. If the EPC was not issued by Pfizer, or if the chip ID does not match the one in Pfizer's records for that EPC, the Authentication Service sends a notice, through the authentication application, to the pharmacist or wholesaler to quarantine the product.

Authentication Service also contacts Pfizer's Medical Information Services, a group of Pfizer employees who process suspected cases of counterfeit drugs and would likely ask the pharmacist or wholesaler to send the suspected bottle of Viagra back to Pfizer for investigation.

The introduction of the RFID inside a company can be seen as a Business Process Reengineering project, and like in every BPR project, not all the functionalities can be implemented from the beginning in the industry, because of the difficulty in managing the change and the high level of costs in implementing the identified solution.
So an effective change management is needed, because the introduction of a new technology requires changes in people behaviour and culture and processes.
As a result, there are many factors that prevent the effective implementation of RFID system; one of the most overlooked obstacles to successful BPR project implementation is resistance from those people more impacted by the change. Most projects underestimate the cultural impact of major process and structural change and as a result, do not achieve the full potential of their change effort.

So it is important to introduce first a pilot project and only after try to extend the technology in every part of the supply chain and to increase the number of functions able to be implemented by this technology.

Surely in the short term it is not possible to introduce the track and trace functionality because of the high cost of the needed technology and the fact that technology is still on his infancy from this point of view, and then really few companies are adopting the tags for this purpose.

By the time when more companies will be using the technology for this aim, its cost is going to be lower.

For example, Gador S.A, a leading pharmaceuticals company based in Argentina, decided to introduce the RFID solution inside its supply chain in order to have more visibility and ensure quality and safety of its products.
The first step in the project was to form a taskforce; several studies and tests simulating the usual processes of packaging the product by Gador**,** were conducted. The pilot project included all stages of packaging process, from item level identification to

complete control of pallets in the production line.

The results of the pilot were extremely successful, confirming the use of RFID technology in the identification of drugs, can be safe tool which does not adversely affect the packaging and logistics processes and at the same time optimizes the traceability of these products unequalled previously.

In the manufacturing process the carton boxes are loaded into the machine that will perform the packaging of the blister packs. At this stage there are two ways to perform the identification of the products with RFID, the first is on an individual basis (or item level) and the second is in bulk. They decided to build a pallet of 360 packs.

So as guarantee the correct traceability of the medications, a correct link must be established between the individual cartons that make up a pack and the pack itself.

Once a pallet with 360 packs (total of 7200 individual cartons) has been created, an RFID pallet Tag must be generated which maintains the relationship between individual carton, pack and pallet. This process requires the correct reading of all the packs that make up a pallet in order to link them with the identification of the pallet in question.

Product safety is a complicated and important issue, as well as a major challenge to global trade. There is much concern in the industry and from its large healthcare clients and their patients, about whether a drug that has been prescribed is authentic or not.
The pharmaceutical industry estimates that between 2 and 7 percent of all drugs sold globally are counterfeited. When a situation like this occurs, there is serious impact on the drug company's share price.

RFID technology makes it easier to ensure that drugs are authentic, and it also creates an electronic pedigree, or record of the chain of custody, from the point of manufacture to the point of dispensing.
Electronic pedigrees will improve patient safety and protect the public health by allowing wholesalers and retailers to rapidly identify, quarantine, and report suspected counterfeit drugs and conduct efficient, targeted recalls.
The use of the combination between EPC and RFID allows the supply chain network to

enhance the track and trace capabilities of product movement and anti-counterfeiting within the supply chain.

One of the obvious strengths of the proposed system is its ability to track and trace the product anywhere and anytime. In particular, the system is not only limited to depicting product supply chain information to authorized parties, but it can also integrate such information with other applications to support decision making and communication.

This new network provides support and consideration for manufacturers in particular to further adopt the application in a global and standardized fashion, so as to realize its full potential as an authentication solution and supply chain analyser.

In conclusion, it is possible to say that the RFID is mainly able to solve most of the problems faced by the pharmaceutical supply chain; this doesn't mean that it is the only viable technology, but it is the most effective one.

# Conclusion

There can be no doubt that the pharmaceutical industry is changing: the maturation of the emerging markets has transformed conventional thinking with regard to business competitiveness, extending the supply chain has become a mainstay of most competitive strategies.
Along with this expansion, the challenges in securing products as they move through the supply chain have continued to escalate. In the U.S., drug diversion and counterfeiting cost this industry approximately 10 percentage of total revenue.
On the other side the FDA has not ignored the issue of securing the expanding supply chain: it issued its first guidance on e-pedigree in 2006.
The basic concept of an e-pedigree is to create a digital audit trail using digital signatures layered one upon the other to demonstrate control and verification at all key phases of the supply chain. Today, several technologies can achieve this type of integrity; from a technology perspective the clear front-runner is RFID.

The promise of RFID is undeniable, but it is important to understand its technological limitations before launching into an RFID implementation. RFID tags can be grouped into four basic categories: passive tags, semi-passive tags, semi-active tags and active tags, as discussed in chapter one. Passive tags are by far the mostly broadly implemented and span several market sectors; these are designed to simply store data that can be read by a reader. They are the lowest priced technology. They do not possess any intelligence or security. On the other hand, active tags typically come equipped with a lithium battery and can emit a signal periodically, these tags can easily cost from $20 to $150 per unit.

Understanding what the supply chain needs is one key element in selecting the appropriate tag: another is recognising the risks of implementation.

So a lot of issues are still to be solved before a full application of this technology will be possible in the pharmaceutical industry and many organisations and governmental

agencies are trying to address these problems, because the pharmaceutical supply chain is critical not only for the industry itself, but even for the whole society.

# References:

Abhisam, RFID systems for pharmaceutical distributors to meet the new FDA regulations on drugs, Pharma 2020

Acierno R., Maffia M., Mainetti L., Patrono L., Urso E. (2011), "RFID-based tracing systems for drugs:Technological aspects and potential exposure risks", Biomedical Wireless Technologies, Networks, and SensingSystems (BioWireleSS), 2011 IEEE Topical Conference on ,Publication Year: 2011 , Page: 87 - 90

Agarwal Ritu, Gao Guodong (Gordon), DesRoches Catherine, Jha Ashish K (2010), "The Digital Transformation of Healthcare: Current Status and the Road Ahead", Information Systems Research, Volume 21, Issue 4

A. C. S. Amaro, A. P. F. D. Barbosa-Po´voa (2008), "Planning and scheduling of industrial supply chains with reverse flows: A real pharmaceutical case study", Computers and Chemical Engineering 32 (2008) 2606–2625

Amini Mehdi, Otondo Robert F., Janz Brian D., Pitts Mitzi G. (2007), "Simulation Modeling and Analysis: A Collateral Application and Exposition of RFIDTechnology.", Production & Operations Management, Vol. 16 Issue 5, p586-598

Tom Andel (2011), "Supply chain visibility", MATERIAL HANDLING & LOGISTICS

Arshinder, Arun Kanda, S.G. Deshmukh (2008), "Supply chain coordination: Perspectives, empirical studies and research directions", International Journal of Production Economics, Volume 115, Issue 2, Pages 316-335

Vivek Bapat, Glenn Restivo (2005), "Reaping the Long-Term Benefits of integrating Radio Frequency identification into the pharmaceutical manufacturing", Pharmaceutical Engineering, May/June 2005

Barchetti U., Bucciero A., De Blasi M., Mainetti L., Patrono L. (2010), “RFID, EPC and B2B convergence towards anitem-level traceability in the pharmaceutical supplychain”, RFID-Technology and Applications (RFID-TA), 2010 IEEE International Conference , Publication Year: 2010 , Page(s): 194 - 199

Mark Barratt, Adegoke Oke (2007), “Antecedents of supply chain visibility in retail supply chains: A resource-based theory perspective”, Journal of Operations Management, Volume 25, Issue 6, Pages 1217-1233

Erkan Bayraktar, Mehmet Demirbag, S.C. Lenny Koh, Ekrem Tatoglu, Halil Zaim (2009), “A causal analysis of the impact of information systems and supply chain management practices on operational performance: Evidence from manufacturing SMEs in Turkey”, International Journal of Production Economics, Volume 122, Issue 1, Pages 133-149

Bernstein Ilisa B. G., Shuren, Jeffrey (2006), “The Food and Drug Administration's Counterfeit Drug Initiative”, Journal of Pharmacy Practice, Volume 19, Issue 4

Tonya Boone, Ram Ganeshan (2007), “The frontiers of eBusiness technology and supply chains”, Journal of Operations Management, Volume 25, Issue 6, Pages 1195-1198

Maurice Bonney, Mohamad Y. Jaber (2011), “Environmentally responsible inventory models: Non-classical models for a non-classical era”, International Journal of Production Economics, Volume 133, Issue 1, Pages 43-53

Youssef Boulaksil, Jan C. Fransoo (2010), “Implications of outsourcing on operations planning: findings from the pharmaceutical industry”, International Journal of Operations & Production Management Vol. 30 No. 10, 2010 pp. 1059-1079

Çakıcı Özden Engin, Groenevelt Harry - Seidmann, Abraham (2011), "Using RFID for the management of pharmaceutical inventory — system optimization and shrinkage control", Decision Support Systems, Volume 51, Issue 4

Catarinucci L., Colella R., De Blasi M., Patrono L., Tarricone L. (2010), "Improving item-level tracing systems through Ad Hoc UHF RFID tags", This paper appears in: Radio and Wireless Symposium (RWS), 2010 IEEE, Issue Date : 10-14 Jan. 2010, page(s): 160 - 163

Celeste Robert, Cusack Beth Ann (2006), "EPCglobal Standards in the Pharmaceutical Industry: Toward a Safe and Secure Supply Chain", Journal of Pharmacy Practice , Volume 19, Issue 4

Michael N. Cook (2006), "Estimating national drug consumption using data at different points in the pharmaceutical supply chain", Pharmacoepidemiology and Drug Safety, Volume 15, Issue 10

Alberto Coustasse, Cody Arvidson & Phil Rutsohn (2010), "Pharmaceutical Counterfeiting and the RFID Technology Intervention", Journal of Hospital Marketing & Public Relations, Volume 20, Issue 2, 2010

Deus, Lucia (2006), "Technological Roles in Combating Drug Diversion and Counterfeiting" Journal of Pharmacy Practice, Volume 19, Issue 3

Sarv Devaraj, Lee Krajewski, Jerry C. Wei (2007), "Impact of eBusiness technologies on operational performance: The role of production information integration in the supply chain", Journal of Operations Management, Volume 25, Issue 6, Pages 1199-1216

Goutam Dutta, Robert Fourer, Akhilesh Majumdar, Debabrata Dutta (2007), "An optimization-based decision support system for strategic planning in a process industry: The case of a pharmaceutical company in India", International Journal of Production Economics, Volume 106, Issue 1, Pages 92-103

Pete Engardio, Arlene Weintraub (2008), “OUTSOURCING THE DRUG INDUSTRY”, SEPTEMBER 15, 2008, BUSINESSWEEK

Geraldo Ferrer, Susan K. Heath, Nicholas Dew (2011), “An RFID application in large job shop remanufacturing operations”, International Journal of Production Economics, Volume 133, Issue 2, Pages 612-621

Geraldo Ferrer, Nicholas Dew, Uday Apte (2010), “When is RFID right for your service?”, International Journal of Production Economics, Volume 124, Issue 2, Pages 414-425

John V. Gray, Aleda V. Roth, Michael J. Leiblein(2011), “Quality risk in offshore manufacturing: Evidence from the pharmaceutical industry”, Journal of Operations Management, Volume 29, Issues 7-8, Pages 737-752

Gray, J., A. Roth, and MJ Leiblein (2011), “Quality Risk in Offshore Manufacturing.” Journal of Operations Management. Vol. 29(7-8): 737-752.

Goldhammer, Alan - Lassman, Scott M. (2006), “Pharmaceutical Supply Chain Security: A View From the Pharmaceutical Research and Manufacturers of America”, Volume 19, Issue 4

Ruggero Golini, Matteo Kalchschmidt (2011), “Moderating the impact of global sourcing on inventories through supply chain management”, International Journal of Production Economics, Volume 133, Issue 1, Pages 86-94

Gunasekaran, E.W.T. Ngai (2005), “Build-to-order supply chain management: a literature review and framework for development”, Journal of Operations Management, Volume 23, Issue 5, Pages 423-451

Tobias Hausen, Melanie Fritz, Gerhard Schiefer (2006), “Potential of electronic trading in complex supply chains: An experimental study”, International Journal of Production Economics, Volume 104, Issue 2, Pages 580-597

Ji Hongen, Chen Yu (2009), “Business Intelligence and RFID in SCM”, Management of e-Commerce and e-Government, 2009. ICMECG '09. International Conference on , Publication Year: 2009 , Page(s): 335 - 338

Manpreet Hora, Hari Bapuji, Aleda V. Roth (2011), “Safety hazard and time to recall: The role of recall strategy, product defect type, and supply chain player in the U.S. toy industry”, Journal of Operations Management, Volume 29, Issues 7-8, Pages 766-777

Huang G.Q., Zhifeng Qin, Ting Qu, Qingyun Dai (2010), “RFID-enabled pharmaceutical regulatory traceability system”, RFID-Technology and Applications (RFID-TA), 2010 IEEE International Conference , Publication Year: 2010 , Page(s): 211 - 216

Jan de Vries, Robbert Huijsman (2011), “Supply chain management in health services: an overview”, Supply Chain Management: An International Journal 16/3 (2011) 159–165

Jan de Vries (2011), “The shaping of inventory systems in health services: A stakeholder analysis”, International Journal of Production Economics, Volume 133, Issue 1, Pages 60-69

Jeng A.B., Li-Chung Chang, Te-En Wei (2009), “Survey and remedy of the technologies used for RFID tags against counterfeiting”, This paper appears in: Machine Learning and Cybernetics, 2009 International Conference on, Issue Date : 12-15 July 2009, Volume : 5, On page(s): 2975 - 2981

Kamran Karbassi (2009), “Analysis and mapping of the supply chain Structure and NPI a new skin Regeneration product into the UK Market”, 2009

Marie Kim, Jae Gak Hwang (2010), “New approach for Convergence of IT + pharmaceutical industry”, This paper appears in: Information and Communication Technology Convergence (ICTC), 2010 International Conference, Issue Date: 17-19 Nov. 2010, page(s): 569 - 570

Brian King, Xiaolan Zhang (2008), “Securing the Pharmaceutical Supply Chain using RFID”,
2007 International Conference on Multimedia and Ubiquitous Engineering (MUE'07)

Kontnik, Lewis T. (2006), “Manufacturer and Industry Responses to the Counterfeiting Challenge”, Journal of Pharmacy Practice, Volume 19, Issue 3

P. Krishna and D. Husak (2007), “RFID infrastructure—a technical overview,” IEEE Applicat. Practice, vol. 1, no. 2, Sep. 2007.

Kate Kuhrt (2008), “The BRIC Countries Opportunities for Regulated Market Players”, PHARMACEUTICAL TECHNOLOGY, outsourcing resouces 2008

S.K. Kwok, S.L. Ting, Albert H.C. Tsang,C.F. Cheung (2010), “A counterfeit network analyzer based on RFID and EPC”, Industrial Management & Data Systems,Vol. 110 Iss: 7, pag.1018 - 1037, 2010

S.K. Kwok, Jacky S.L. Ting, Albert H.C. Tsang, W.B. Lee, Benny C.F. Cheung (2010), “Design and development of a mobile EPC-RFID-based self-validation system (MESS) for product authentication”, presented at Computers in Industry, 2010, pp.624-635.

Law Elaine, Youmans Sharon (2011), “Combating Counterfeit Medications: The California Pharmacist Perspective”, Journal of Pharmacy Practice, Volume 24, Issue 1

Lybecker Kristina M. (2008), “Keeping it real: anticounterfeiting strategies in the pharmaceutical industry”, Managerial and Decision Economics, Volume 29, Issue 5

Ann Marucheck, Noel Greis, Carlos Mena, Linning Cai (2011), “Product safety and security in the global supply chain: Issues, challenges and research opportunities”, Journal of Operations Management, Volume 29, Issues 7-8, Pages 707-720

Ann Marucheck, Noel Greis, Carlos Mena, Linning Cai (2011), “Insights on the Special Issue on Product Safety and Security in the Global Supply Chain Journal of Operations Management”, Volume 29, Issues 7-8, Pages 704-706

Jim Miller (2009), “The Future of Pharmaceutical CMC Outsourcing”, PHARMACEUTICAL TECHNOLOGY, outsourcing resouces 2009

Stefan Minner (2001), “Strategic safety stocks in reverse logistics supply chains”, International Journal of Production Economics, Volume 71, Issues 1-3, Pages 417-428

Alan Minsk, Diana Rusk (2009), “An ounce of prevention: Dealing with the threat of counterfeit pharmaceuticals”, Journal Pharmaceuticals Policy and Law, Volume 11, Number 3, 2009, Pages 153-159

A. Mousavi, M. Sarhadi, S. Fawcett, S. Bowles, M. York (2005), “Tracking and traceability solution using a novel material handling system”, Innovative Food Science & Emerging Technologies, Volume 6, Issue 1, Pages 91-105

Shah Nilay (2004), “Pharmaceutical supply chains: key issues and strategies for optimisation” Computers and Chemical Engineering, Volume 28, Issue 6/7

Roger Parloff (2004), “The new drug war”, Fortune, March 8, 2004http://money.cnn.com/magazines/fortune

Marcelo Caldeira Pedroso, Davi Nakano (2009), “Knowledge and information flows in supply chains: A study on pharmaceutical companies”, International Journal of Production Economics, Volume 122, Issue 1, Pages 376-384

Potdar M., Sharif A., Potdar V., Chang, E. (2009), “Applications of Wireless Sensor Networks inPharmaceutical Industry”, Advanced Information Networking and Applications Workshops, 2009. WAINA '09. International Conference on , Publication Year: 2009 , Page(s): 642 - 647

Manohar Potdar, Elizabeth Chang, Vidyasagar Potdar (2006), “Applications of RFID in Pharmaceutical Industry”, This paper appears in: Industrial Technology, 2006. ICIT 2006. IEEE International Conference, Issue Date : 15-17 Dec. 2006, pag. 2860 - 2865

Ranky P (2007), “Engineering Management-Focused Radio Frequency Identification (RFID) Model Solutions”, IEEE Engineering Management Review, Volume 35, Issue 2

Jennifer Shang, Tuba Pinar Yildirim, Pandu Tadikamalla, Vikas Mittal, Lawrence H. Brown (2009), “Distribution Network Redesign for Marketing Competitiveness”, Journal of Marketing, Vol. 73 (March 2009), 146–163

Matthieu-P. Schapranow, Juergen Mueller, Alexander Zeier, Hasso Plattner (2010), “Sustainable use of RFID Tags in the Pharmaceutical Industry”, This paper appears in: Smart Objects: Systems, Technologies and Applications (RFID Sys Tech), 2010 European Workshop on, Issue Date: 15-16 June 2010, On page(s): 1 - 7, Date of Current Version: 01 giugno 2011

Schwarz Leroy, Zhao Hui (2011), “The Unexpected Impact of Information Sharing on US Pharmaceutical Supply Chains”, Institute for Operations Research and the Management Sciences, Volume 41, Issue 4, Pag.354-364

Rui T. Sousa, Songsong Liu, Lazaros G. Papageorgiou, Nilay Shah (2011), “Global supply chain planning for pharmaceuticals”, chemical engineering research and design 89 (2011) 2396–2409

Cheri Speier, Judith M. Whipple, David J. Closs, M. Douglas Voss (2011),"Global supply chain design considerations: Mitigating product safety and security risks", Journal of Operations Management, Volume 29, Issues 7-8, Pages 721-736

Yao-Hua Tan, Niels Bjørn-Andersen, Stefan Klein (2010), "Accelerating Global Supply Chains with IT-Innovation" ITAIDE Tools and Methods

Ting S.L., Kwok S.K., Tsang A.H.C., Lee W.B. (2010), "Enhancing the information transmission forpharmaceutical supply chain based on RadioFrequency Identification (RFID) and Internet of Things", IEEE CONFERENCES, Supply Chain Management and Information Systems (SCMIS), 2010 8th International Conference

Shiou-Fen Tzeng, Wun-Hwa Chen, Fan-Yun Pai (2008), "Evaluating the business value of RFID: Evidence from five case studies", International Journal of Production Economics, Volume 112, Issue 2, Pages 601-613

Charles Conrad Uy, Gerhard Symons (2007), "Hits Like a BRIC How to make sense of the growing diabetes market in Brazii, Russia, India, and China", Pharmaceutical Executive, Publish date: Oct 1, 2007

Uysal I., DeHay P.W., Altunbas E., Emond J.-P., Rasmussen R.S., Ulrich D. (2010), "Non-thermal effects of radio frequency exposure on biologic pharmaceuticals for RFID applications", This paper appears in: RFID, 2010 IEEE International Conference

Shawnee K. Vickery, Robert E. Markland (1985), "Integer goal programming for multistage lot sizing: Experimentation and implementation", Journal of Operations Management, Volume 5, Issue 2, Pages 169-182

Samuel Fosso Wamba, Louis A. Lefebvre, Ygal Bendavid, Élisabeth Lefebvre (2008), "Exploring the impact of RFID technology and the EPC network on mobile B2B eCommerce: A case study in the retail industry", International Journal of Production Economics, Volume 112, Issue 2, Pages 614-629

Wang, D. Li, C. O'brien, Y. Li (2010), "A production planning model to reduce risk and improve operations management", International Journal of Production Economics, Volume 124, Issue 2, Pages 463-474

Meilin Wang, Qingyun Dai, Xiangwei Zhang, Xiong Luo, Runyang Zhong (2010), "A RFID-enabled MES for real-time pharmaceutical manufacturing supervision", This paper appears in: RFID-Technology and Applications (RFID-TA), 2010 IEEE International Conference, Issue Date17-19 June 2010, pag. 194 - 199

Weinstein R. (2005), "RFID: a technical overview and its application to the enterprise", IT Professional, Volume: 7 Issue:3, May-June 2005

Wigand R.T., Mande D.M., Wood J.D (2011), "Information Management and Tracking of Drugs in Supply Chains within the Pharmaceutical Industry", Information Management and Tracking of Drugs inSupply Chains within the Pharmaceutical Industry, Information Technology: New Generations (ITNG), 2011 Eighth International Conference on , Publication Year: 2011 , Page(s): 500 - 507.

W.K. Wong, S.Y.S. Leung, Z.X. Guo, X.H. Zeng, P.Y. Mok (2011), "Intelligent product cross-selling system with radio frequency identification technology for retailing", International Journal of Production Economics, (In Press, Corrected Proof, Available online 31 August 2011)

David C. Wyld (2008), "Genuine medicine?", competitiveness review: an international business journal, Volume 18, Issue 3, 2008, pp. 206-216

Xuan Yu, Cheng Li, Yuhua Shi, Min Yu (2010), "Pharmaceutical supply chain in China: Current issues and implications for health system reform", Health Policy 97 (2010) 8–15

Dianmin Yue, Xiaodan Wu, Junbo Bai (2008), "RFID Application Framework for pharmaceutical supply chain", Service Operations and Logistics, and Informatics, 2008.

IEEE/SOLI 2008. IEEE International Conference,; Issue 12-15, pag. 1125 - 1130

Allan N. Zhang, Mark Goh, Fanwen Meng (2011), "Conceptual modelling for supply chain inventory visibility", International Journal of Production Economics, Volume 133, Issue 2, Pages 578-585

EPCglobal US COMMENT DHHS, ANTI-COUNTERFEIT DRUG INITIATIVE WORKSHOP, FEBRUARY, 2006

Anonymous (2005), "Follow The Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain", The Health Strategies Consultancy, March 2005

"Tech Startup Uses Cell Phones To Root Out Counterfeit Drugs", Forbes, May 17, 2011, Helen Coster

# Web reference (last visited on 2nd december 2011):


[1] http://www.rfidjournal.com/article/view/1336, 2005 RFID Journal

[2] http://www.rfidjournal.com/article/view/1337, 2005 RFID Journal

[3] http://www.rfidjournal.com/article/view/1339, 2005 RFID Journal

[4] http://www.rfidjournal.com/article/view/1334, 2005 RFID Journal

[5] http://www.rfidjournal.com/article/view/1332, 2005 RFID Journal

[6] http://www-01.ibm.com/software/success/cssdb.nsf/CS/JHAL-7UMFV6?OpenDocument&Site=gicss67alnc&cty=en_us

[7] http://www-01.ibm.com/software/success/cssdb.nsf/CS/STRD-7HHGC2?OpenDocument&Site=gicss67alnc&cty=en_us

[8] http://www.ibm.com/ibm/ideasfromibm/us/rfid/061207/RFID_10012008.pdf

[9] http://en.wikipedia.org/wiki/Radio-frequency_identification

[10] http://www.industrial-ebooks.com/EBOOK/pharmaceutical-RFID-systems.pdf

[11] http://www.contractpharma.com/issues/2006-01/view_features/anti-counterfeiting-initiatives-and-rfid-practices/

[12] http://www.alientechnology.com/docs/SB_RFID_Retail.pdf

[13] http://www.impinj.com/Applications/Solutions_Powered_by_Impinj.aspx# Pharmaceutical Industry

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