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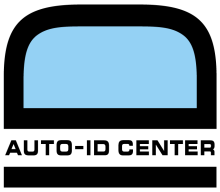


# WHITE PAPER

## Securing the Pharmaceutical Supply Chain

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## ABSTRACT

The complexity of the United States health care system is increasing rapidly. Demographic changes, along with a host of new drugs, are causing greater volumes of raw materials and finished products to move through the pharmaceutical supply chain. Because drugs are expensive, there is always the possibility of counterfeit. Several recent cases of counterfeit medicines have raised American awareness of the problem. Auto-ID technology provides an effective information infrastructure to detect and control counterfeit drugs through track and trace and drug verification capabilities.

# WHITE PAPER

## Securing the Pharmaceutical Supply Chain

## Biographies

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Associate Director

Robin Koh has over 12 years of supply chain industry experience in North America, Europe and Asia. He has held Director positions at Arrow Electronics and Pepsi-Cola International. He has a Bachelors in Industrial Engineering and Operations Research from the University of Massachusetts at Amherst, an MBA from the Tuck School of Business at Dartmouth College and a Masters in Engineering from the Massachusetts Institute of Technology.

**Edmund W. Schuster**
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Edmund W. Schuster has held the appointment of director of the Affiliates Program in Logistics at the Massachusetts Institute of Technology and is currently working on MIT Auto-ID projects. Before MIT, Ed spent 20 years in the food industry working for Welch's and Oscar Mayer in various corporate logistics and operations management positions. He has a Bachelors of Science in food technology from the Ohio State university and a Master of Public Administration, emphasis in management science, from Gannon University. Ed is a fellow of the American Production and Inventory Control Society.

  

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## Securing the Pharmaceutical Supply Chain

## Biographies

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Research Associate

Indy Chakrabarti graduated from Rice University in 1997 with a Bachelors in Science in Electrical and Computer Engineering. He received his Masters in Logistics from MIT in 2003.
Mr. Chakrabarti has five years of experience in the technology industry helping architect and sell enterprise software solutions. He is currently employed at security software company, NetIQ, in Houston, Texas.

**Attilio Bellman**
Research Associate

Attilio Bellman has worked in the field of logistics and supply chain management for the last six years. He was Product Manager at Optimum Logistics, Director of Global Logistics Services for Americas at Danzas-AEI and, prior to that, International Officer at United Nations. He has a Master of Engineering in Logistics from the Massachusetts Institute of Technology and a PhD in Solid State Physics from University of Milan His work at the Auto-ID Center focuses on the application of the Auto-ID technology and infrastructure to the pharmaceutical and health care industries.

# WHITE PAPER

## Securing the Pharmaceutical Supply Chain

### Contents

# 1. INTRODUCTION

The complexity of the United States health care system is increasing rapidly. Demographic changes, along with a host of new drugs, are causing greater volumes of raw materials and finished products to move through the pharmaceutical supply chain. In many ways, the pharmaceutical supply chain is beginning to resemble the distribution of consumer goods (Cottrill 2001). However, several important differences remain.

The fundamental goal of the medical industry is patient care and safety. To achieve these goals for the public good, the Food and Drug Administration (FDA) and individual States regulate the industry through laws and administrative orders designed to protect the integrity of drugs throughout the pharmaceutical supply chain. These laws and regulations require millions of pages of information to document the flow of drugs from manufacture to consumption (Mitchell 1998).

Implicit in the documentation process is the administrative requirement to do track and trace. **Tracking** involves knowing the physical location of a particular drug within the supply chain at all times. **Tracing** is the ability to know the historical locations, the time spent at each location, record of ownership, packaging configurations and environmental storage conditions for a particular drug.

Track and trace forms the foundation for improved patient safety by giving manufacturers, distributors and pharmacies a systemic method to detect and control counterfeiting, drug diversions and mishandling. These are important aspects of supply chain security. Unfortunately, the current system for the documentation and organization of data is cumbersome because of a reliance on manual procedures and storage of information on paper. As a practical result, track and trace takes place only in an emergency such as a drug recall.

Auto-ID technology offers the prospect for an integrated solution to the track and trace problem. The open standards feature of the technology aids in the implementation of a supply chain wide application. In addition, Auto-ID sets the foundation for a number of other applications within the health care industry (Brock 2002).

The next section examines the scope of the counterfeit problem and the legal underpinnings for improved trace and trace capabilities within the pharmaceutical supply chain.

# 2. AN INTERNATIONAL PROBLEM OF SIGNIFICANT MAGNITUDE

The WHO defines Counterfeit as "A medicine that is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging."[1]

[1] World Health Organization (Feb 15, 2003). http://www.who.int/medicines/organization/qsm/activities/qualityassurance/counterfeit/faq_counterfeit.doc

According to the WHO definition, what makes a drug/medicine counterfeit is the deliberate or intentional (criminal) nature of the mislabeling or adulteration of a drug. This type of illegal behavior leads to 1) compromises of patient safety, 2) economic loss to established drug manufacturers, and 3) a threat to the national security of sovereign countries.

The WHO estimates that **between five and eight percent** of the worldwide trade in pharmaceuticals is counterfeit.[2] Many industry experts believe this to be a conservative estimate. Anecdotal reports indicate a significant increase in counterfeit drugs during the past few years.

[2] "Pharmaceutical Product Tampering News Media Factsheet," HDMA (March 2003).

A few examples of published articles on counterfeit include:

- "Up to 33% of anti-malarial drugs for sale in Cambodia, Laos, Burma, Thailand and Vietnam contained no active ingredient"
  **The Lancet, 6/19/2001**

- "Approximately 192,000 people died in China in 2001 due to the effects of counterfeit drugs. As much as 40% of drugs in China are counterfeit."
  **The Washington Post, 8/30/02**

- "In Columbia, up to 40% of medications are believed to be counterfeit."
  **U.S. News & World Report, 6/11/01**

- "Approximately 50% of drugs sold in Nigeria are counterfeit."
  **IFPW Focus, 6/13/02**

- In a study conducted simultaneously at Dulles and Oakland International Airports, U.S. Customs and FDA agents found that 10% of the drugs they analyzed contained no active ingredients.
  **U.S. News & World Report, 6/11/01**

The problem of counterfeit drugs has reached grass roots America. Pharmacist Lowell Anderson of Bel-Aire Pharmacy in White Bear Lake, MN states, "I have been in this business for 40 years…I have less confidence in the integrity of the supply chain today than ever before. It scares me."[3] This appears to be a well-founded concern. During the past ten years, drugs sold in America such as Procrit, Epogen, Serostim, Zyprexa, Diflucan, Combivir and Retrovir have been counterfeited. Even Lipitor, the widely prescribed drug to control cholesterol levels, was recalled recently because of a counterfeiting incident. In this particular case, the FDA could not determine how many bottles were in each of three counterfeit lots. As well, the current destination of the counterfeit lots could not be determined. While most counterfeit drugs contain harmless ingredients such as water or glucose, the counterfeiting of Lipitor "posed a potentially significant health hazard" according to the FDA.

3 "Fake drugs show up in U.S. pharmacies ; As prescription prices rise, counterfeiters chase profits." USA TODAY; McLean, Va – (May 15, 2003); written by Julie Appleby.

Even though the overwhelming majority of drugs sold in the United States are safe, the $192 billion per year pharmaceutical market is an attractive target for counterfeiters. With the complete mapping of the Human Genome, there will be a number of new, high priced drugs appearing on the market during the next few years. This will increase the opportunity for counterfeit.

## 2.1. The Causes of Counterfeit

Three factors account for the increase in counterfeit drugs:[4] First, the computer technology available to forge labels has become more sophisticated. It is now possible to reproduce any label. Second, there is an abundance of small wholesalers buying and selling medications. Along with differences in pricing, the increase in small wholesalers creates an active secondary, or gray market. In some situations, drugs change hands many times before reaching pharmacies. This increases the opportunity to introduce counterfeit into the supply chain. Finally, an increased number of expensive drug therapies provide lucrative potential for forgers to net large profits. In some cases, organized crime and former illicit drug dealers have entered the counterfeit ethical drug market because the profit potential is so large.

4 "Fake drugs show up in U.S. pharmacies ; As prescription prices rise, counterfeiters chase profits." USA TODAY; McLean, Va – (May 15, 2003); written by Julie Appleby.

Federal efforts to deal with counterfeit are hindered by laws that do not assign supply chain wide accountability to any one authority. Re-importation and diversion, in addition to the advent of internet pharmacies, makes counterfeit hard to prevent. In summary, it is not very difficult to produce a counterfeit drug for introduction into the United States pharmaceutical supply chain. The incentive is great for criminals to take part in this illegal activity.

### 2.2. The Changing Regulatory Environment

With greater awareness of counterfeit drugs, the FDA and states are moving forward with new legislation to combat the problem. Florida recently gained national attention by introducing a legislative bill to establish a "pedigree" for each drug sold in the state (Chackrabarti 2003). The intention of the bill is to verify authenticity and reduce the chance of counterfeit. Though this bill has not yet become law, it introduces a number of important issues for the pharmaceutical industry to consider.

Specifically, the bill calls for the following information to accompany each drug through all steps of the supply chain:

1. Drug Name
2. Dosage
3. Container size
4. Number of containers
5. Drugs Lot or Control numbers
6. Business Name and Address of ALL parties to each prior transaction, starting w/the manufacturer
7. The date of each previous transaction

These requirements add a great deal of complexity for manufacturers and distributors. As an example, the typical drug distributor carries up to 40,000 stock keeping units. Maintaining pedigrees given this volume of drugs is overwhelming with current identification and information technology.

Other countries besides the United States have moved forward with pedigree regulations. Most notably the Italian government, with financial support from the European Union, began in 2000 to enforce the track and trace of pharmaceuticals through the Bollini Law. This law requires application of a special sticker containing a serial number and bar code to each unit of sale.

The Bollini Law also requires all parties within the supply chain to record and archive each serial number. This has created great difficulty for manufacturers and distributors. As a result, the full implementation of the law will not take place until June 2004 because of a lack of technology to handle the task of recording and archiving the serial numbers. A complete design of the database structure needed to do track and trace has not yet been determined. Open questions remain about the role of the Italian government in controlling and maintaining a large-scale central database containing all drug pedigree information. In an average year, Italian distributors handle 1.2 billion items. It remains uncertain how bar code technology and existing information processing infrastructure will cope with this much data.

## 3. CURRENT SOLUTIONS TO THE PHARMACEUTICAL COUNTERFEIT PROBLEM

In response to regulatory and business pressures, the pharmaceutical industry attempts to combat counterfeit using a number of different techniques. To date, no technique has proven effective in eliminating the problem. Most detection procedures currently in place rely on manual product inspection by pharmacists or sales representatives to check for evidence of counterfeiting. In the absence of automated inspection technology, these methods are often too costly to do counterfeit inspection on a broad, periodic basis. If positive detection of counterfeit does occur, it is not clear what action to take because current methods provide incomplete information about the scope of counterfeiting for a particular drug.

Recent efforts to deal with counterfeit involve both information and material technologies. Several examples include:

- Some drug companies have injected an inert chemical signature directly into medications, which can be checked with a small handheld device much like a home pregnancy test
  **U.S. News & World Report, 6/11/01**

- Tamper proof packaging, in addition to technical measures such as holograms, difficult to replicate packaging designs, and unique fonts have been used.

- FDA Medwatch **(www.fda.gov/medwatch/index.html)** is an excellent resource for patient safety information, from label changes to counterfeit product warnings and recalls.

- HDMA Product Safety Task Force **(www.healthcaredistribution.org)** recommends steps and guidelines the industry should consider for the safe purchase of products.

- The Institute for Safe Medication Practices **(www.ismp.org)** is dedicated to the safe use of medications through improvements in drug distribution, naming, packaging, labeling, and delivery system design.

- Product Surety **(www.productsurety.org)** is a joint industry initiative with the FDA to curb the incidence of counterfeiting.

Product anti-Counterfeit technologies fall into two broad categories; covert or overt, and intra-formulary versus package based.[5] There are a large number of these technologies in use today. Listed in the table below are the most commonly used technologies and an assessment about the chances of defeating each approach:

[5] Protecting Medicines & Pharmaceuticals, 2002.

**Table 1**

| ANTI-COUNTERFEIT MEASURE | COVERT | OVERT | REPLICATION |
|---|---|---|---|
| **Intra-Formulation** | | | |
| Immunoassay | ✓ | | Low |
| Unique Flavoring | | ✓ | Low |
| **Package Level** | | | |
| Design | | ✓ | High |
| Watermarks | ✓ | ✓ | High |
| Digital Watermarks | ✓ | ✓ | New |
| Fibers and Threads | ✓ | ✓ | Medium |
| Reactive Inks | ✓ | ✓ | Medium |
| Holograms, OVD | ✓ | ✓ | High |
| Bar Code | | ✓ | High |

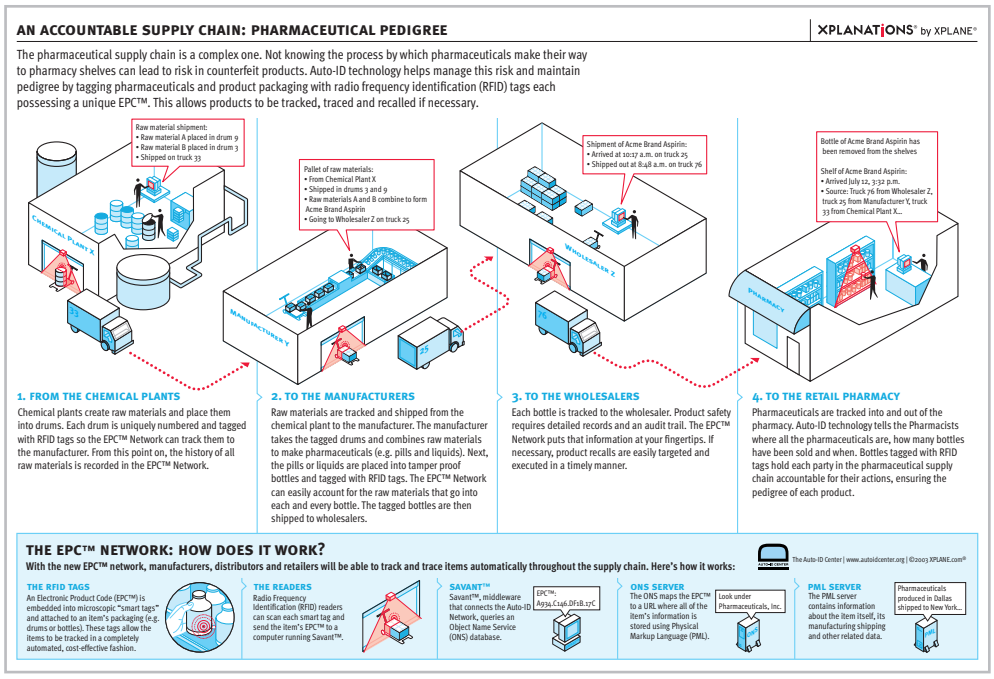
These approaches are static. Manufacturers replicate the approach many times to cover millions of individual dosages for a specific drug. After a particular anti-counterfeiting solution has been in the market for some time, counterfeiters learn ways to defeat the safeguard. Manufacturers constantly have to remain a step ahead by either adopting new measures or mixing and matching current technologies. While the changing of anti-counterfeit approaches helps manufacturers and regulatory agencies differentiate genuine product from false product, the rapid changes are confusing to the public at large. This creates a situation where consumers have a difficult time checking the authenticity of a product themselves.

# 4. AN ANTI-COUNTERFEIT SYSTEM BASED ON INFORMATION

Auto-ID technology enables two fundamental, supply chain wide approaches to deal with counterfeit drugs. Both of these approaches compliment the current overt and covert techniques employed by the pharmaceutical industry. First, Auto-ID technology allows the possibility of instant verification for any drug, at any location. This verification process is possible through a proposed information technology infrastructure that spans the complete supply chain. Second, Auto-ID technology allows the ability to do robust track and trace. This capability provides true pedigree information about drugs, accessible by supply chain partners. Together, track and trace, and drug verification, are difficult barriers for potential counterfeiters to overcome.

Both approaches depend on the capability to identify individual drugs within the supply chain at the primary package level. RFID tags, containing an EPC™, applied to each unit of dosage provides this capability. Figure 1 outlines a conceptual framework for an Auto-ID implementation in a typical pharmaceutical supply chain. The diagram shows how each element of Auto-ID technology, RFID tags, readers, the Savant, ONS and the PML server fit together to form an integrated solution that achieves unique identification of individual drugs. For a complete overview of Auto-ID technology, see Engels et al. (2003).

**Figure 1**




The Auto-ID approach has advantages as compared to bar codes when doing track and trace or drug verification. Using bar code systems to read the billions of identifiers needed to record location and serial number information for individual drugs suffers from several limitations. First, bar codes require a line of sight to do a proper read. For serialized drugs individually labeled with bar codes at the primary package level, and shipped in cartons, direct reads are laborious. In addition, bar codes can only provide unidirectional information, i.e. an item cannot be remotely "asked" to communicate information such as location, or temperature, for recording in an enterprise resource planning (ERP) system database.

The appeal of Auto-ID technology lies in the ability to use the EPC™ as a pointer to look up important information about a drug that is contained in a remote database. Either the Internet or dedicated computer networks can provide the communication link. This ability to link physical objects to information provides a powerful capability for track and trace, and drug authentication. However, this new capability does have drawbacks. The task of handling streaming information for billions of individual pharmaceutical products taxes the capacity of the Internet or dedicated computer networks. Section 4.2 discusses approaches to overcome this capacity concern.

## 4.1. An Example of Pharmaceutical Supply Chain Complexity

Figure 1 infers that the form of the physical goods can change during each step of the pharmaceutical manufacturing and distribution process. Immediately after completion of each step, the product becomes a finished good that continues as an input to the next step in the supply chain.

Referring to Figure 1, the finished product for the chemical plant is bulk active ingredient packaged in drums with a specific name, composition, lot number, and expiration date. In contrast, the transport carrier that moves the drums of active ingredient from the chemical plant to the manufacturer sees only a shipment of specific weight and volume. Other attributes are not important to the carrier. There is no direct, continuous link to attributes of the shipment such as lot number or expiration date.

To deal with this situation, pharmaceutical manufacturers have placed select pieces of information directly onto the package by printing bar codes or lot numbers. In this case, the package becomes the vehicle for carrying the information needed for track and trace, and authenticity verification through the supply chain. Though the information carrying capacity of this approach is limited, it does guarantee universal access to all parties within the supply chain. Unfortunately, this "self contained" approach of physically attaching information to the secondary package can be, and often is counterfeited. In addition, information contained on the secondary package is hard to access quickly on a meaningful scale. This limits possibilities for serialization of drugs at the secondary package level. As a compromise, pharmaceutical manufacturers often rely on assigning lot numbers to large amounts of drugs that might exceed one hour of production. However, this practice lacks the granularity needed for the supply chain of the future.

The process of identity change continues throughout each step of the supply chain making drug verification, and track and trace, difficult to accomplish even with the self-contained approach for transmitting information. Historically, pharmaceutical manufacturers and distributors have gathered the information needed for drug authentication, and track and trace, using detailed forms and secure databases as storage devices. In even the best situations, this information is difficult to retrieve and seldom shared with other parties outside of the firm. In the event of a recall, special teams within firms are charged with the task of accessing data to make important decisions about the extent of the problem. This is usually a labor-intensive process.

## 4.2. Aggregation and Inheritance

Although the physical form of goods changes throughout manufacturing and distribution, a link still exists for all raw materials and work in process used to produce finished goods. This type of link demonstrates inheritance of specific attributes. Each medicine used by the patient has a specific lot number and expiration date printed on the container. The drug is shipped on a specific truck, at a specific temperature for a specific duration. The effectiveness of the medicine ultimately depends on the quality of the manufacturing process and the environmental conditions of transport and storage. These are all inherited attributes.

Organizing the large number of informational links for drugs in the supply chain requires adherence to two concepts:

**Data Aggregation** is the logical equivalent of item aggregation or assembly. By viewing data within a supply chain as a series of parent – child relationships, track and trace becomes possible.

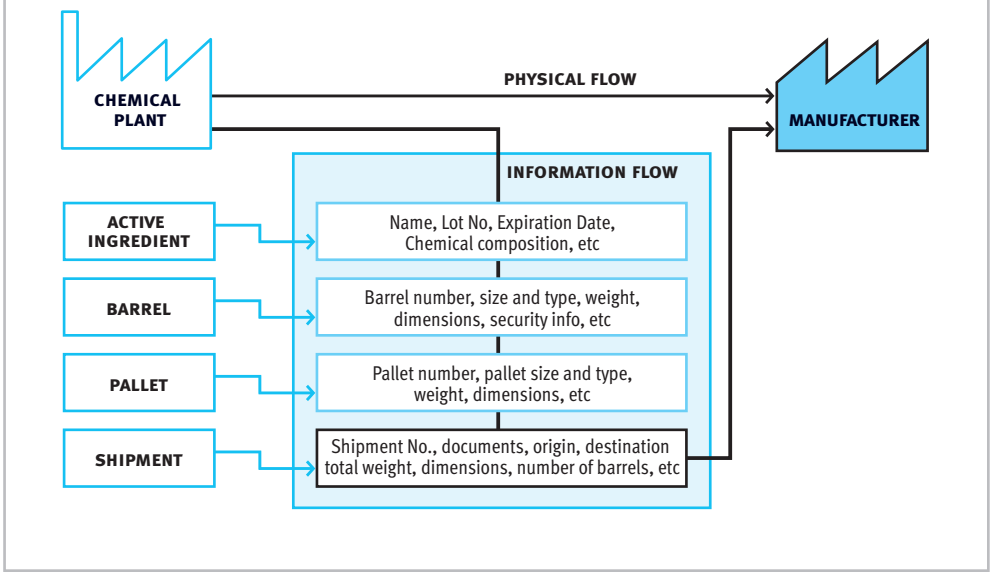
**Data Inheritance** is the history of the parent data. To reconstruct the history of an item, each change in form must transfer from parent to child.

Data aggregation reduces the number readings at critical points within the supply chain, making capture of informational links needed for large-scale drug verification, and track and trace, feasible. This becomes evident when dealing with pallet level shipments. Adopting the concept of data aggregation and inheritance allows the opportunity to read a single RFID tag, fixed to a pallet, for specific details about each product on the pallet. If data aggregation was not possible, the RFID tag for each product on the pallet would need to be read, resulting in a great deal of additional reads.

Figure 2 shows a visualization of data aggregation for the flow of information between a chemical plant and the manufacturer represented in Figure 1. In this case, information flow is in parallel to physical product flow. The information infrastructure built by the Auto-ID center takes advantage of data aggregation and inheritance.

Figure 2

**EXAMPLE OF INFORMATION AGGREGATION**




Several articles provide technical details about how Savant, EPC™, PML and ONS work together to make track and trace possible (Dinning and Schuster 2003; Floerkemeier and Koh 2002; Milne 2002 a & b; Chang et al. 2002).

### 4.3. The Flow of Information within a Pharmaceutical Supply Chain

The underlying theory of logistics depends on the flow of information for effective management. In particular, the information flow between two physical locations must synchronize with the parallel flow of goods. **Data pre-positioning** or the use of a **central repository** within the supply chain are important concepts that simplify the synchronization process (Milne 2002a, Harrison et al. 2003).

As an example to explain information flows, consider the data needed for shipments between two firms. Finished products in the consumer goods and pharmaceutical industries typically are packed into cases that in turn are loaded onto pallets. A complete shipment consists of a specific number of pallets. Each shipment has an identification number, a bill of lading number, a quantity of pallets, an invoice number, an origin and destination, a driver, and a truck ID number.

Assume that each individual unit, carton or pallet contains an EPC™ embedded in an RFID chip. When scanned, the EPC™ number is linked by the ONS to specific information about the item accessible through the Internet or other type of computer network (Milne 2002 a & b). To synchronize the flow of both goods and information the shipper must either 1) send in advance (pre-position) complete PML files containing all the information regarding the objects to be received (the **thick file** approach), 2) preposition only EPCs™ (the **thin file** approach) or 3) write select information to a third party for use by supply chain partners. These alternatives represent different ways to share important information within the supply chain.

For drug verification, only EPC™ validation is necessary. This is binary, yes/no information. However, for track and trace purposes transfer of additional information that is dynamic must occur. This information might include:

- Origin
- Destination
- Time stamps
- Company names
- Telemetry information – temperature and humidity

For track and trace, location information is extremely important because it provides 1) the past position of the goods, 2) present position of the goods and 3) the anticipated future position of the goods (assuming a scheduled shipment exists). Time stamps at each location allow the calculation of residence time.

## 5. AN AUTO-ID BASED SOLUTION

This section deals with the specific information infrastructure needed for the two alternatives to combat counterfeit; track and trace, and drug authentication. Building on the principles of data aggregation and inheritance, the goal is to gain complete supply chain visibility for detection and control of counterfeit. The outcome of such an approach is a robust information infrastructure that provides anti-counterfeit measures to deal with three major categories:

- **Completely fake Product**
- **Tampered Product**
  - Adulteration
  - Substitution
- **Unacceptable status of the Product**
  - Including, Expired, Discarded, Returned, Recalled, And Samples

Two components of Auto-ID technology form the backbone of supply chain wide visibility. As Harrison et al. (2003) state, "The key to the Auto-ID architecture is the Electronic Product Code™, which extends the granularity of identity data far beyond that which is currently achieved by most barcode systems in use today." In addition, the PML servers, located at each node of the supply chain, and secure Internet based communication combine to provide the primary information handling structure and means.

Both hardware components, the EPC™ tags and PML servers, are technologically feasible with significant development having taken place during the past four years. In the case of EPC™ tags, encryption technology, the ability to sense and record temperature and humidity, and the ability to sense certain types of tampering are recent advances that fit nicely with the anti-counterfeit mission. A cadre of vendors is capable of producing these two infrastructure components in sufficient supplies to meet demands of the pharmaceutical industry. As commercial volumes of production occur, costs will decrease because of learning curve effects. In summary, Auto-ID technology is ready for the challenges of large-scale commercial application.

In preparation for a detailed analysis of drug verification and track and trace, the next section discusses three important databases that will handle the storage and transfer of information.

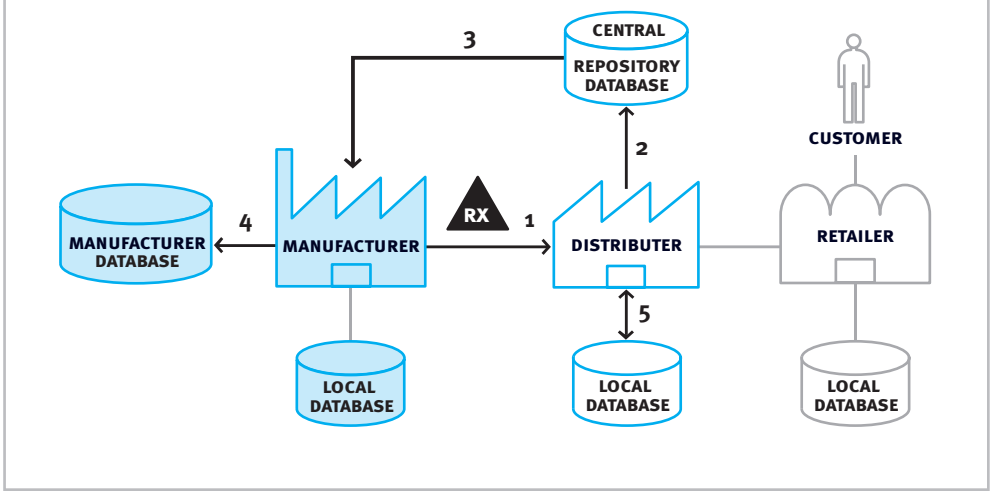
## 5.1. Database Overview

The proposed Auto-ID technology solution to counterfeit is comprised of three different types of databases with access levels restricted based on business rules defined by supply chain partners. The **Manufacturer Database** contains information about a particular drug and a potential link to product registries such as the Red Book or First Interstate catalogs. The **Central Repository Database** contains the trail of all exchanges for a drug in the supply chain. Administered through a 3rd party, this database contains only select information from manufacturers and distributors needed to secure the supply chain. Finally, the **Local Database** contains information important to the manufacturer or distributor handling the drug. This might include such information as the warehouse location for an individual drug, or management signatures indicating completion of critical procedures. This information is important only to the organization in possession of the drug. Figure 3 provides a schematic of all three databases within the pharmaceutical supply chain.

**Figure 3:**

1 Arrival of product from manufacturer
2 Query for authenticity
3 Redirect query to manufacturer
4 Manufacturer verifies authenticity
5 Distributor accepts item and begins local tracking

**DIAGRAM OF RF-ENABLED SUPPLY CHAIN**



With this supply chain wide view, a broad categorization of information exists:

**Static** – information that does not change through time (ex. Product size and weights)
**Semi Dynamic** – information that changes with long time intervals (lot numbers based on production run)
**Dynamic** – information that changes with short time intervals (location, temperature, pressure and humidity readings)

The manufacturer database contains static and semi-dynamic information. In the Auto-ID view, a subset of this database is made available for supply chain wide access using several means, including secure Internet access. In turn, the repository database contains predominantly EPCs™ and related location and timestamp information obtained from nodes within the supply chain. This information is available to all who have security clearance. Finally, the local database contains dynamic information; some of which might also be written to the repository database.

## 5.2. Counterfeit Detection within an Auto-ID Enabled Supply Chain

With the Auto-ID infrastructure in place track and trace, and drug verification, becomes possible. The final section of this paper examines how Auto-ID enables these important pharmaceutical supply chain security measures.

### 5.2.1. Track and Trace

Harrison et al. (2003) put forth the following design for a supply chain wide central repository database.

**Figure 4:**

= Data packet:
- EPC™
- Arrival/release time
- Custodian ID
- EPC™ to track in future (Empty Schema of type of data stored)

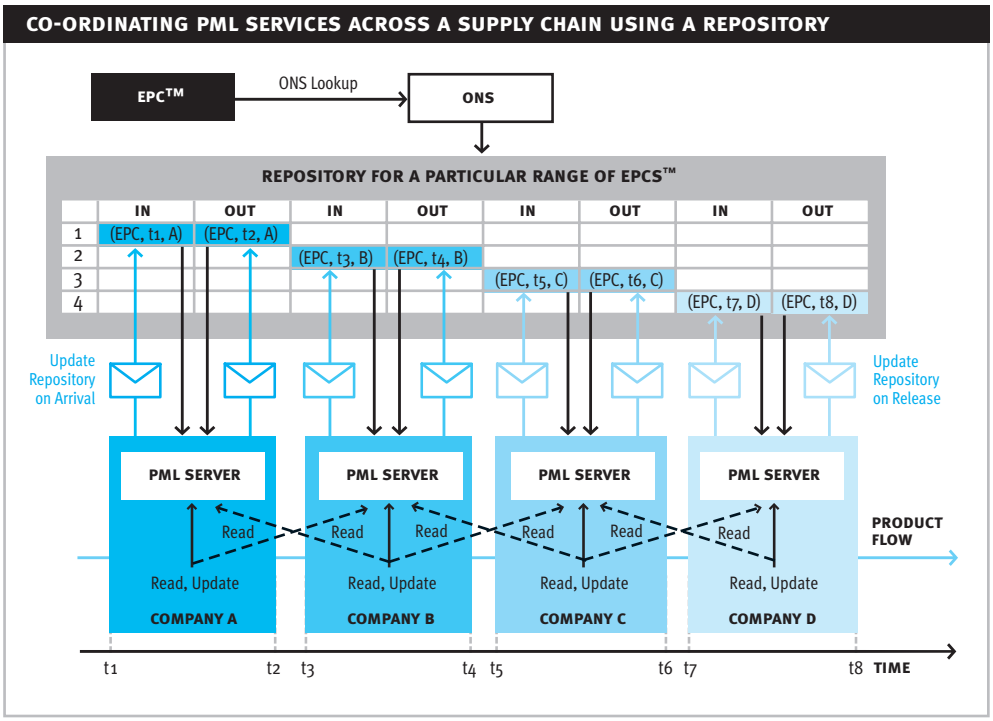



Figure 4 shows a supply chain representation with PML Servers as the backbone for routing information. The four step supply chain example in the diagram is analogous to the pharmaceutical supply chain representation given in figure 1, with Company A,B, C, & D corresponding to 1) The Chemical Plant, 2) The Manufacturer, 3) The Wholesaler and 4) The Retail Pharmacy.

In this scenario, information needed for a drug pedigree is written into the central repository from each node in the supply chain. The concepts of aggregation and inheritance reduces the amount of data reported to the repository by associating groups of EPCs™ with activities that occur at each supply chain node such as storage and shipping. Writing the pedigree information to a single database also increases accessibility to all parties within the supply chain. Real time query is possible.

In contrast to the central repository approach, using a second method, pre-positioning, where information moves sequentially through PML servers as drugs are shipped means that current pedigrees are only available at the farthest point of progress through the supply chain. Information pre-positioning does provide effective tracking capabilities for shipments between two nodes, however, trace information requires following pointers backward through PML servers located in the separate business organizations that make up the pharmaceutical supply chain. This would appear to limit real time access to pedigree information and make supply chain wide telemetric information hard to consolidate.

In summary, the central repository approach proposed in Harrison et al. (2003) provides a more robust solution in creating supply chain wide pedigrees for drugs. With Auto-ID based pedigrees, there will be systematic, timely, and targeted ways to build information for every drug.

#### 5.2.2. Drug Verification

In contrast to building an information infrastructure for pedigrees that depends on a 3rd party repository, drug verification is a simpler case. The informational focus of drug verification centers on the PML files located at the manufacturer. The process of verifying a drug is binary. Either the drug is authentic or it is counterfeit. A thin subset of PML files that contain only valid EPCs™, and current status, could be extracted from PML servers and posted for secure internet access. No other information except valid EPCs™ would be listed. Other supply chain organizations, such as wholesalers and pharmacies could scan the EPCs™ contained on drugs and compare to valid EPCs™ posted by the manufacturer. Any discrepancies would be a strong indication of counterfeit. In this situation, no pedigree information is available, so it is possible that a valid EPC™ could be mishandled or adulterated as it passes out of the control of the manufacturer. To deal with these issues, Auto-ID will utilize sophisticated anti-tamper tags and integrate with current anti-tampering packaging methods to ensure the physical product is secure.

In summary, drug verification requires a much simpler information infrastructure; however, the approach does not provide as much security. It is possible that implementation of drug verification might be a first step toward obtaining full track and trace capability needed for complete drug pedigrees.

## 6. CONCLUSION

Both track and trace, and drug verification are feasible through the implementation of Auto-ID technology. While application of Auto-ID technology to combat counterfeit is compelling, several factors offer complexities that must be overcome.

The Auto-ID approach assumes that all drug manufacturers, carriers, wholesalers and pharmacies have the necessary hardware and computing ability to read and process EPC™ information. It is unrealistic to believe that this capability will occur immediately. However, through recent merger activity, the number of players in the pharmaceutical industry has decreased. This situation could make the job of implementing an industry wide Auto-ID solution to detect and control counterfeit easier because there are fewer major players.

The Auto-ID approach would have to be fine-tuned in terms of information synchronization among many different supply chain partners to ensure a high level of reliability for pedigree and drug verification information. If a single supply chain partner did not properly handle information, pedigrees might show gaps that would raise counterfeit questions. The Auto-ID approach assumes different entities within the pharmaceutical supply chain can achieve a common level of cooperation in supporting the information infrastructure.

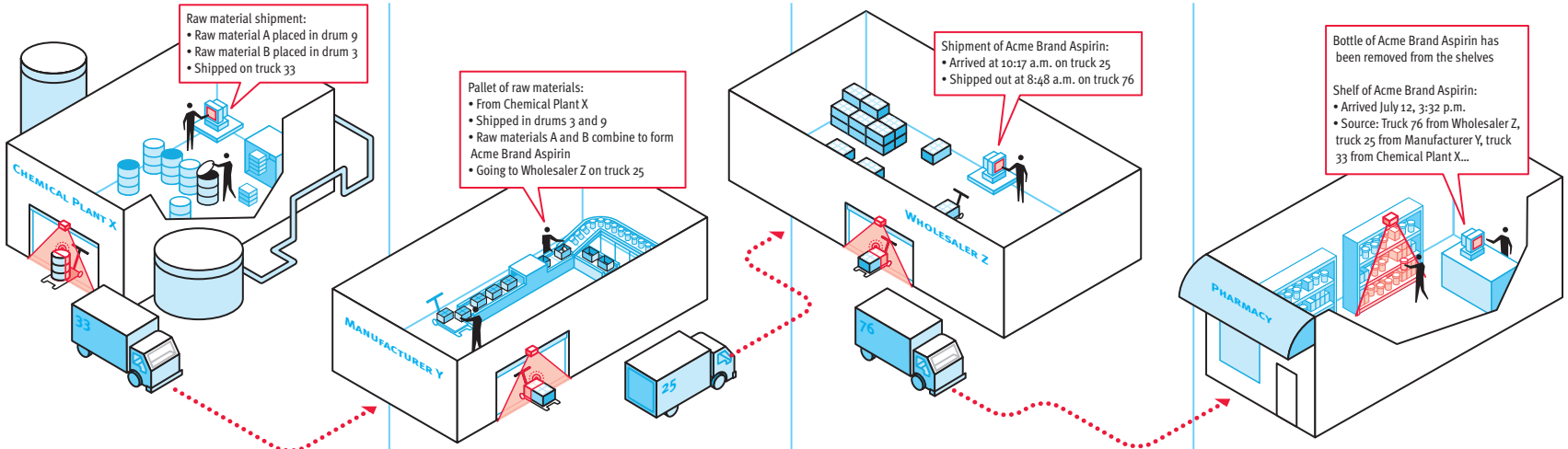
Besides proposed applications in improving track and trace, and drug verification, Auto-ID infrastructure also serves as the foundation for future applications of importance to the health care industry.

For example, the Human Genome Project creates greater opportunities for engineering drugs to treat small groups of individuals that suffer from specific illnesses (Philipkoski 2003). These “designer drugs” will be manufactured in small lot sizes on a make to order basis. In this environment, logistics and coordination takes a new form as thousands of biotechnology drugs flood the pharmaceutical supply chain. Delivery of these new drugs to the right group of people presents a challenge that the current logistical system cannot handle effectively. Auto-ID lays the foundation for the management of this not-to-distant complexity and provides the framework for a Safer and Securer Supply Chain.

## AN ACCOUNTABLE SUPPLY CHAIN: PHARMACEUTICAL PEDIGREE

XPLANATIONS® by XPLANE®

The pharmaceutical supply chain is a complex one. Not knowing the process by which pharmaceuticals make their way to pharmacy shelves can lead to risk in counterfeit products. Auto-ID technology helps manage this risk and maintain pedigree by tagging pharmaceuticals and product packaging with radio frequency identification (RFID) tags each possessing a unique EPC™. This allows products to be tracked, traced and recalled if necessary.




### 1. FROM THE CHEMICAL PLANTS

Chemical plants create raw materials and place them into drums. Each drum is uniquely numbered and tagged with RFID tags so the EPC™ Network can track them to the manufacturer. From this point on, the history of all raw materials is recorded in the EPC™ Network.

### 2. TO THE MANUFACTURERS

Raw materials are tracked and shipped from the chemical plant to the manufacturer. The manufacturer takes the tagged drums and combines raw materials to make pharmaceuticals (e.g. pills and liquids). Next, the pills or liquids are placed into tamper proof bottles and tagged with RFID tags. The EPC™ Network can easily account for the raw materials that go into each and every bottle. The tagged bottles are then shipped to wholesalers.

### 3. TO THE WHOLESALERS

Each bottle is tracked to the wholesaler. Product safety requires detailed records and an audit trail. The EPC™ Network puts that information at your fingertips. If necessary, product recalls are easily targeted and executed in a timely manner.

### 4. TO THE RETAIL PHARMACY

Pharmaceuticals are tracked into and out of the pharmacy. Auto-ID technology tells the Pharmacists where all the pharmaceuticals are, how many bottles have been sold and when. Bottles tagged with RFID tags hold each party in the pharmaceutical supply chain accountable for their actions, ensuring the pedigree of each product.

## THE EPC™ NETWORK: HOW DOES IT WORK?

**With the new EPC™ network, manufacturers, distributors and retailers will be able to track and trace items automatically throughout the supply chain. Here's how it works:**

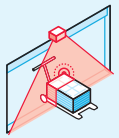


#### THE RFID TAGS

An Electronic Product Code (EPC™) is embedded into microscopic "smart tags" and attached to an item's packaging (e.g. drums or bottles). These tags allow the items to be tracked in a completely automated, cost-effective fashion.

#### THE READERS

Radio Frequency Identification (RFID) readers can scan each smart tag and send the item's EPC™ to a computer running Savant™.

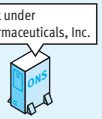


#### SAVANT™

Savant™, middleware that connects the Auto-ID Network, queries an Object Name Service (ONS) database.


#### ONS SERVER

The ONS maps the EPC™ to a URL where all of the item's information is stored using Physical Markup Language (PML).




#### PML SERVER

The PML server contains information about the item itself, its manufacturing shipping and other related data.

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