

Technological strategies to deal with counterfeit medicines: the European and North-American perspectives

Elisabeth Lefebvre, Alejandro Romero, Louis-A. Lefebvre and Caroline Krissi

Abstract— The magnitude of counterfeit medicines represents a serious and increasingly rising international concern. In fact, it is estimated that 10% of the pharmaceutical products sold worldwide are counterfeited. The scope of counterfeited medicines is equally worrisome since counterfeiting activities target both branded and generic products as well as non-prescription medicines to life-saving drugs. It is therefore critical for the stakeholders of different pharmaceutical supply chains to elaborate and develop effective technological strategies to combat the phenomenon of counterfeit medicines. This paper examines the effectiveness of such strategies from both the European and North American perspectives.

Keywords—Counterfeit medicines, Pharmaceutical supply chain, the End-to-end verification system, E-pedigree system, 2D barcode Data Matrix, RFID.

I. INTRODUCTION

COUNTERFEIT medicines are considered as a major growing health and safety issue [1] with deep financial and non-financial consequences for the pharmaceutical industry, the governments and the final consumers. In terms of financial consequences, counterfeit medicines represent 10% of the medicines commercialized around the world [2] for an estimated value of 75 billion US dollars in 2010 [2], [4]. Pharmaceutical companies are thus deprived of their return on R&D investments and see their revenues decrease while

Manuscript received January 1st, 2011.

Elisabeth Lefebvre is full professor and co-director of ePoly, center of expertise from École Polytechnique de Montréal, Mathematics and Industrial Engineering Department, P.O. Box 6079, Station Centre-ville Montréal, Canada, H3C 3A7 (e-mail: elisabeth.lefebvre@polymtl.ca).

Alejandro Romero is a PhD candidate from École Polytechnique de Montréal, Mathematics and Industrial Engineering Department, P.O. Box 6079, Station Centre-ville Montreal, Canada, H3C 3A7 (e-mail: alejandro.romero@polymtl.ca).

Louis A. Lefebvre is associate professor and director of the ePoly, center of expertise from École Polytechnique de Montréal, Mathematics and Industrial Engineering Department, P.O. Box 6079, Station Centre-ville Montréal, Canada, H3C 3A7 (e-mail: Louis.a.lefebvre@polymtl.ca).

Caroline Krissi is a research assistant from École Polytechnique de Montréal, Mathematics and Industrial Engineering Department, P.O. Box 6079, Station Centre-ville Montreal, Canada, H3C 3A7 (e-mail: caroline.krissi@polymtl.ca).

governments cannot perceive corporate taxes on these lost revenues. Employment in the legal pharmaceutical supply chain is adversely affected and exports decrease. Finally, both public and private entities incur additional expenses to control these illicit counterfeiting activities [5]. Problems with counterfeit pharmaceuticals go beyond the financial dimension and are difficult to assess since counterfeit medicines have also a negative impact on the innovation in the industry, on the reputation of pharmaceutical companies, on the brand value and on the trust of the general public. Moreover, counterfeit medicines raise serious health risks and compromise patient safety [6]. In 2009, 1 700 incidents related to the counterfeit medicines were reported to the *Pharmaceutical Security Institute PSI* [3]. These products contain insufficient active ingredients, and in some cases, toxic or hazardous ingredients [7]. The effects of counterfeit medicines range from a modest clinical improvement to severe health problems resulting in multiple deaths [4]. For instance, in early 2008, the death of 149 patients in the US was linked to an adulterated anti-coagulant called heparin [8].

Several initiatives to fight counterfeit medicines are undertaken and can be summarized along three perspectives: (1) the improvement of the existing legislative and regulatory framework, (2) the communication efforts to increase the awareness from all stakeholders, including the final customers who may face serious health risks from counterfeit medicines and (3) the elaboration of technological strategies for the authentication of genuine medicines and the detection of counterfeit medicines, namely the end-to-end verification system vs. E-pedigree system.

This paper focuses on the technological initiatives undertaken by the stakeholders of different pharmaceutical supply chains. More specifically, we will analyse the overall technological strategies and the two competing technologies which are envisioned to act as data carriers, namely the two-dimensional barcode called *Data Matrix*, and the Radio Frequency IDentification (*RFID*) tag. We will also present some empirical evidence from 72 European and North-American organizations in order to assess the effectiveness of these technological strategies.

II. BACKGROUND

A counterfeit medicine is defined as “a medicine deliberately and fraudulently mislabelled with respect to identity and/or source” [4]. It may include the wrong

ingredients, or contain no or inefficient active ingredients for both branded and generic products, from non-prescription medicines to life-saving drugs, and, for medicines sold by virtual pharmacies on the Internet or medicines obtained from the hospitals' pharmacies. Technological solutions retained for fighting counterfeit medicines attempt to offer three levels of protection [10]. At the first level, the integrity of primary and secondary package is ensured by tamper-evident features: for example, security seals, glue with perforated cartons and carton folding box with breakage evidence. At the second level, pharmaceutical products are authenticated by covert and overt technologies such as immunoassay, chemical tagants, reactive inks, holograms, watermarks, color shifting inks, guilloches, fibres or threads. At the third and last level of protection, each medicine is identified through the pharmaceutical supply chain using a data carrier. The technological strategies for this third level of protection ensure mass serialization of medicines necessary for tracing medicines at unit level and are analyzed in the next section.

A. Overall technological strategies

Figure 1 presents the two technological strategies that correspond to the third level of protection. The **end-to-end verification system**, as proposed by EFPIA, consists in verifying the authenticity of medicines at the point of dispensing as it is illustrated in Figure 1. Pharmaceutical products are serialized at unit level and recorded in an on-line database by manufacturers. The dispensing pharmacy connects to the central online database, reads the code and compares the read data with the information registered by the manufacturer. Indeed, the dispensing pharmacy validates that 1) "the product record exists and matches the data held on the product itself", 2) "the product record has not been previously marked as dispensed", and 3) "the product record does not contain any warnings or advisory notices" [11]. As manufacturers and retail pharmacies must have access to the on-line database

using XML language, security, privacy and accessibility are key concerns to ensure the functionality of the end-to-end verification system [12].

The FDA as well as the Florida and California governments have initially mandated the adoption of the **e-pedigree system**. This second technological strategy consists in tracing and tracking the medicines at each layer of the pharmaceutical supply chain (bottom part of Figure 2). The manufacturers serialize pharmaceutical products at unit level and all the stakeholders in the supply chain then record the financial transactions and physical movements of medicines at unit level in an on-line database [6], [12]. The chain of custody of pharmaceutical products is therefore set up from the upstream side to the downstream side of the supply chain. Any incongruence in the on-line history of one particular medicine could indicate that this product has been introduced in the chain illegally.

B. The two data carriers

Both the End-to-end verification system and the E-pedigree system depend on the technology that could ensure the mass serialization of pharmaceutical products. The data carrier must have more data capacity than the traditional 1D barcode because it must hold the manufacturer product code, the batch number, the expiration data, the serialization number and extra information [13]. Two technological solutions are proposed as data carriers: (1) the "old" well proven and well accepted technology based on barcodes, namely the 2D barcode *Data Matrix* and (2) the "new" technology, namely RFID.

EFPIA proposes a common European standard for mass serialisation and traceability. This standard is a two-dimensional barcode called *Data Matrix*, more specifically the *2D Data Matrix ECC200* [11]. *Data Matrix* (top part of Figure 2) respects GSI standards and contains the following information: the product code (GTIN), the serial number (Ser), the expiry date, the batch code and additional information

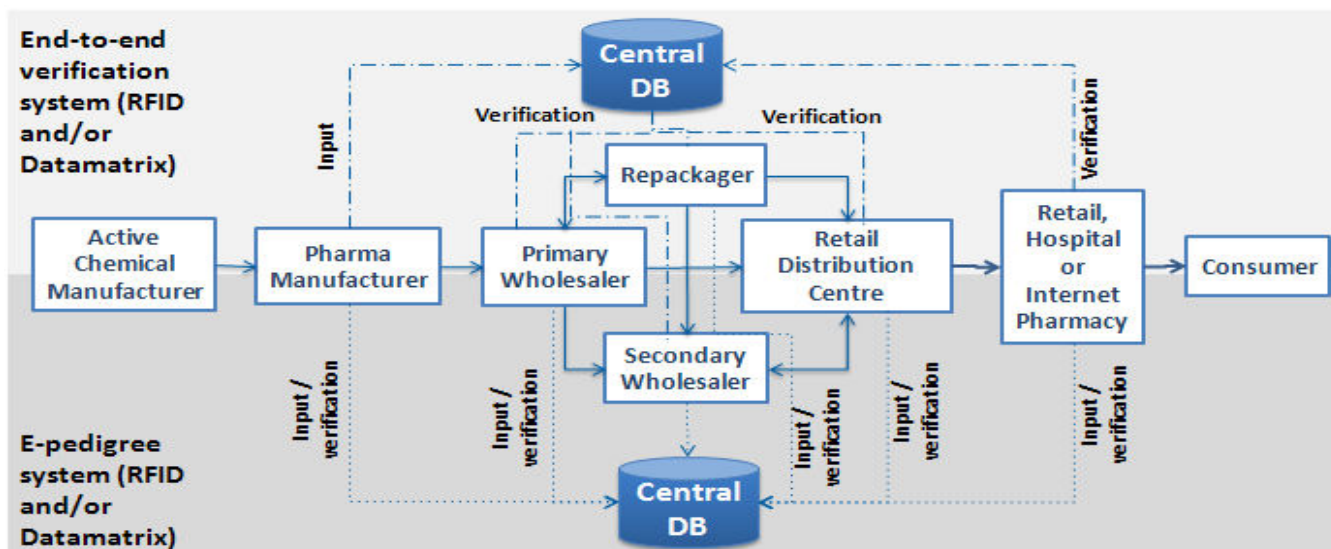


Fig. 1 End-to-end verification system versus E-pedigree system

[11]. This barcode can carry an important amount of data on a small space [55], has a low cost and is compatible with existing processes and with legacy technologies [10]. The information is read manually by direct line of sight [14], [55] and is then transmitted to a middleware before being transferred to a central on-line database (top side of Figure 2). This barcode is usually associated with the end-to-end verification system.

As early as 2004, FDA proposed to adopt **Radio Frequency Identification (RFID)** technologies to track and trace pharmaceutical products [1]. The RFID tags can ensure mass serialization because it can carry the product code, serial number, expiry date, batch code as well as the transactional and commercial information on pharmaceutical products (bottom part of Figure 2). The RFID tag transmits this data directly and without direct line of sight to a reader by radio frequency [14], [53], [54]. Then, the reader transfers this information to the middleware for its transmission to a central on-line database. This technology provides the capacity of tracking any pharmaceutical product at any location through supply chain [15], [6], [56] and holds the potential to improve logistical operations [16], [13], [53]. Indeed, RFID has been intensively adopted in healthcare industry for improving quality of care and reducing medical errors [17]. The EPC Global proposed the GS1 EPCglobal Electronic Pedigree Standard for mass serializing medicines at item level and for recording pharmaceutical transactions into an on-line database using the *Drug Pedigree Messaging Standard DMPS* based on XML language [6]. RFID is typically related to the E-pedigree system.

C. Data Matrix and RFID as competing technologies

As noted by Henderson [18], “old” technologies may be particularly resilient as they are not easily replaced by new ones. Although previous work has offered considerable conceptual insight into the transition between technological generations (i.e. between the old or the new technologies), for example in the form of series of intersecting S-curves based on performance improvements over time, “surprisingly, the interregnum between successive generations has received little attention” [19, p.382]. The specific focus of this paper is to address this under investigated issue by gaining a better understanding of the dynamics of the “interregnum” between the barcode technology and RFID.

New technology often promises more than it can deliver and RFID is no exception as RFID has been qualified as the “key to automate everything” [20], as “one of the ten greatest contributory technologies of the 21st century” [21], and as “the next wave of the IT revolution” [22]. *RFID* may be far more than technological hype as it emerges as a powerful, disrupting and major undertaking [23], [24] spreading over industries in different continents. However, *RFID* does not seem to eclipse its rival “old” technology as it faces a number of challenges that have little to do with its technical performance. First, several entities, agencies and organizations, appear to experience the well-known lock-in phenomenon [25] since the barcode technology has been omnipresent for several decades. Second, *RFID* faces relatively high knowledge barriers that may not be necessarily lowered by the proliferation of *RFID* infrastructure providers, IT consultants and other service firms. Third, the adoption of *RFID* is community driven and is therefore largely determined by the dynamics of the community. It involves important adopters interdependencies [26]. *RFID* adoption in pharmaceutical supply chains is indeed deeply intertwined with organizational and inter-organizational issues and is basically affected by the adoption pattern of its supply chain members. The emergence of a critical mass is determinant for wider adoption but the very complexity of the pharmaceutical supply chains (Figure 3) and the fact that these chains are not fully integrated [27] hamper the emergence of a critical mass.

Because of invested interest, some entities have acted unilaterally. In order to protect the probably most counterfeited medicine, namely Viagra, Pfizer decided to tag all Viagra items with RFID technology for the U.S. market. Because this company loses tens of millions of dollars to the counterfeit drug trade each year, they have invested more than 5 millions of dollars in testing the potential of this technology [6]. In Europe, EFPIA conducted a pilot project to validate the functionality and performance of *Data Matrix*. In the greater Stockholm area, 110,000 units were recorded with *Data Matrix* code and distributed to 25 retail pharmacies. The preliminary results of this project show the efficiency of this technology to protect the integrity of medicines [10].

Some organizations such as *Authentix* and *Nosco* have explored **hybrid technological solutions** for carrying medicine information. These initiatives attempt to combine the respective limitations and the potential of both *Data Matrix* and *RFID*. For example, cases and pallets can be tracked with *RFID* tags, while medicines can be with *Data Matrix*.

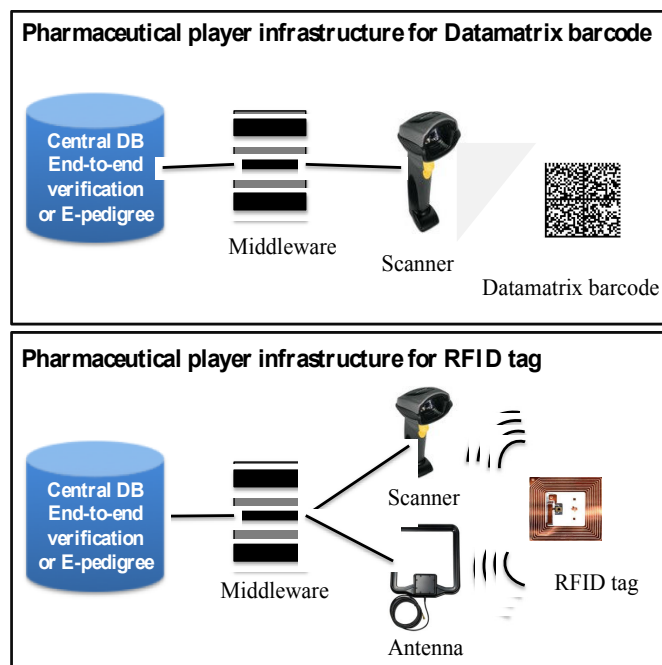


Fig. 2 The respective infrastructure for the two data carriers (Data Matrix barcode vs. RFID)

Pharmaceutical players read only information of cases and pallets and can track medicines at unit level by inheritance and parent-child relationships between items, cases and pallets.

From the above discussion, it can be assessed that no dominant platform using Data Matrix, RFID or both technologies as data carriers has yet emerged. This has prompted us to gather empirical evidence to better understand the technological position of the pharmaceutical supply chain players based in Europe and North America.

III. METHODOLOGY

The research design that corresponds to an exploratory research initiative includes three distinct and complementary phases.

The first phase consists of an in-depth analysis of publicly available information in order to 1) appropriately understand the structure of a standard pharmaceutical supply chain, 2) identify the supply chain members and analyse their role and responsibilities and 3) investigate the penetration of counterfeit medicines in the supply chain. The main observations derived from this first phase are summarized in Figure 3.

The structure of a standard pharmaceutical supply chain includes seven layers (Figure 3). Using different chemical ingredients obtained from *active pharmaceutical ingredients manufacturers* (first layer), medicines are produced by manufacturing entities (*pharmaceutical manufacturers*-second layer). Medicines are then delivered to *primary wholesalers* (third layer) for stocking and retransferring to *secondary wholesalers* (fourth layer) and are, in certain cases, repackaged before being shipped to the *retail distribution center* (fifth layer). From the retail distribution centers, medicines are distributed to final retailers, namely a *retail pharmacy*, a *hospital pharmacy* or an *Internet pharmacy* (sixth layer). These pharmacies represent the point of contact with the consumers (seventh layer).

The supply chain structure as illustrated in Figure 3 may vary slightly depending on the existing relationships between players, the presence of new entrants, the characteristics of different medicines, and the geographical location [28]. For example, wholesalers' activities are highly concentrated in the USA where *McKesson*, *Cardinal Health* and *Amerisource Bergen* distribute 90% of medicines [6]. New entrants such as on-line or Internet pharmacies tend to bypass the established structure as a medicine can be distributed directly to the consumers, a phenomenon that grows each year as a result of consumer interest in commodity and competitive prices [29]. For instance, the sales of medicines by on-line pharmacies in the U.S. represented approximately 20 billion dollars for 2004 [30]. Other stakeholders, in particular associations, governmental entities and technology suppliers and consultants (see bottom part of Figure 1) also play an active and essential role in the adoption and diffusion of technological strategies to fight counterfeit medicines.

Counterfeit medicines can enter in almost any layer of the pharmaceutical supply chain (upper part of Figure 3). The Internet pharmacies are especially a concern since at least 50%

of medicines sold through Internet are counterfeited, mishandled or dated [2]. By analysing more than one hundred pharmacies and thirty prescription-only medicines, the European Alliance for Access to Safe Medicines (EAASM) concludes that "62% of medicines purchased online are fake or substandard (including medicines indicated to treat serious conditions such as cardiovascular and respiratory disease, neurological disorders, and mental health conditions) and 95.6% of online pharmacies researched are operating illegally [31]. However, counterfeit medicines are also found in other layers of the supply chain. For instance, in 2008 the California government examined the medical stock of 500 hospital pharmacies. They found that 18% of hospital pharmacies had counterfeit medicines [8].

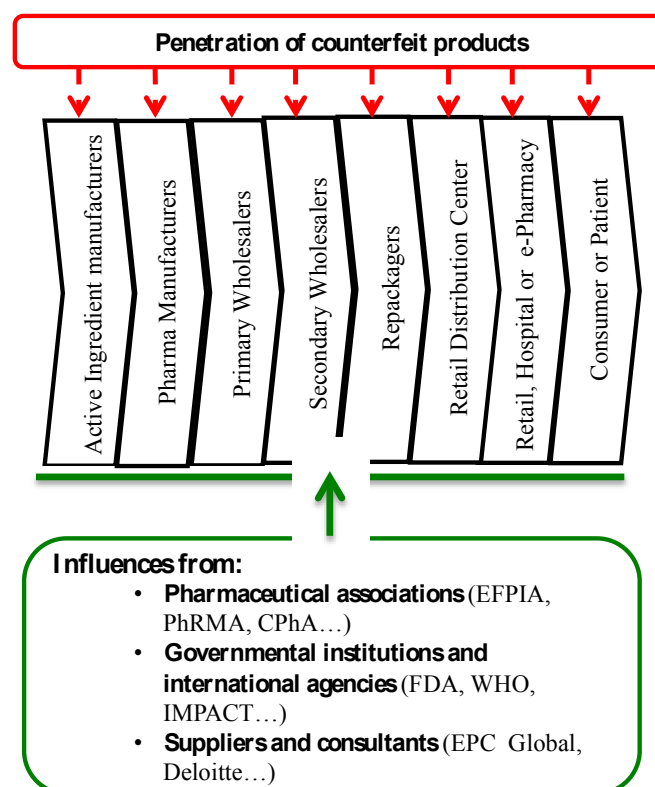


Fig. 3: The structure of a standard pharmaceutical supply chain and the potential penetration of counterfeit medicines

The second phase of the research design represents a field study which targeted knowledgeable managers from different organizations directly involved in the phenomenon of counterfeit medicines (Figure 3) and located in Europe and North-America. On-site structured interviews were conducted with thirty-two (32) respondents from Europe and North America. When potential respondents could not be interviewed on-site due to their busy schedules or their distant geographical locations, an on-line questionnaire proved to be a less costly and more efficient way to reach them. Open-ended questions in the questionnaire provided the possibility for the respondents to give their comments. Thirty-nine (39) respondents provided their input on the on-line questionnaire. A total of 72 organizations thus participated to the study

(Table1). Both regions, namely Europe and North America, display a critical mass of respondents (34 vs. 38 respondents). Respondents from active ingredients manufacturers and pharmaceutical manufacturers (18 firms) to pharmacies (6 organisations) are representative of the pharmaceutical supply chain structure. Other stakeholders such as technology suppliers, consultants, associations and governmental institutions also participated to the study.

The empirical data collected from both the on site-site interviews and the on line questionnaire belong to three broad sets of research variables. The first set represents the contextual variables, namely the level of awareness of counterfeit medicines and the relative effectiveness of existing legislative framework. The second set of variables focuses on the effectiveness of overall technological strategies. The third and last set captures the relative merits of the two data carriers, namely Data Matrix and RFID. The theoretical justification of all research variables arise from a detailed literature review and is particularly pertinent for assessing the merits of the data carriers (see Appendix 1)

The third phase of the research design will be carried out in the next months and will examine in details the corporate and technological strategies of the members of two pharmaceutical supply chains.

The next section presents some preliminary results from the second phase.

IV. RESULTS AND DISCUSSION

A. The existing context

As displayed in Table I, the 72 respondents are very conscious and knowledgeable of the phenomenon of counterfeit pharmaceutical products (4,57) and their own organizations, although to slightly less extent, are also quite aware of such phenomenon (4,28). This validates to a certain extent the choice of respondents and organizations in this study. However, we fully acknowledge that this is based on self-rating.

The current progression of counterfeit medicines is rapid (3,92) and the actual overall legal environment is considered as rather ineffective, either with respect to legislation (2,60), enforcement (2,43) or penal sanctions (2,14). The organizations from our sample have changed to some extent their business strategies to combat counterfeiting (3,85). The observed gap between knowledge (i.e. organizational awareness) and action (i.e. change in organizational strategy) is symptomatic of the difficulties for identifying, tracing and tracking counterfeited pharmaceutical products.

TABLE I
CONTEXT VARIABLES (N=72)

Context variables	Mean
Personal awareness of counterfeit medicines (1)	4,57
Organizational awareness of counterfeit medicines (1)	4,28

Current progression of counterfeit medicines (2)	3,92
Change in organizational strategy to take into account the counterfeit medicines (3)	3,85
Legislation effectiveness against counterfeit medicines (4)	2,60
Enforcement effectiveness against counterfeit medicines (4)	2,43
Penal sanctions effectiveness against the counterfeit medicines (4)	2,14

1) Means based on Likert scales where 1 = not aware, 5 = very aware

2) Means based on Likert scales where 1 = very slow, 5 = very rapid

3) Means based on Likert scales where 1 = not at all, 5 = very much

4) Means based on Likert scales where 1 = not efficient, 5 = very efficient

B. The relative effectiveness of the overall technological strategies

Because the elaboration of the overall technological strategies seems to respond to some geo-political logic (section II. Background), we have divided our sample into two groups in order to compare the position of European organizations to the one held by North-American organizations. T-tests were conducted to test the presence of significant differences between Europeans and North Americans.

As discussed in section 2.3, a common technological strategy has not yet emerged. Instead, multiple possibilities combining the *E-pedigree – track & trace system* and the *End-to-end verification system* with either or both data carriers are being assessed. Table II lists all possible combinations in an attempt to determine the preferred technological strategies in Europe and North America and displays the mean value for each region.

Several interesting observations can be made from the results presented in Table III:

1) Key players in Europe consider that the End-to-end verification system is significantly more effective than the E-pedigree system, which rather congruent with the position held by European governmental agencies and associations.

2) Surprisingly, North American respondents seem rather reserved concerning the effectiveness of both the *E-pedigree system* (3,29) and the *End-to-end verification system* (3,46). In fact, the mean for the *E-pedigree system* is quite low, despite the fact that such a system was initially mandated by the FDA. The publicized drawbacks and the repetitive legislature postponements such as the California's e-pedigree largely explain the North American position. In general, Europe is more optimistic concerning both systems (3,84 vs. 4,03 respectively).

3) When turning to the efficiency of the two data carriers, Europeans rate significantly *Data Matrix* as a more effective data carrier for mass serialisation than *RFID*, while North Americans remain ambivalent with either data Matrix or RFID as it can be deducted from the very similar means (3,32 and 3,34).

4) Of all possible combinations between the two systems and the two data carriers, North Americans tend to prefer

TABLE II
 THE EFFECTIVENESS OF TECHNOLOGICAL STRATEGIES

Effectiveness of different technological strategies	Europe (n=34)	North America (n=38)	
<i>Overall technological strategies</i>			
End-to-end verification system effectiveness	4,03	3,29	***
E-pedigree – track & trace system effectiveness	3,84	3,46	
<i>Data carriers</i>			
Data Matrix barcode effectiveness	4,00	3,32	***
RFID effectiveness	3,75	3,34	
<i>Combining the two systems with the two data carriers</i>			
Data Matrix barcode as enabler of the End-to-end	3,81	3,68	
Data Matrix barcode as enabler of the E-pedigree	3,69	3,73	
RFID & Data Matrix barcode as enabler of the End-to-end	3,68	3,87	
RFID as enabler of the E-pedigree	3,97	3,97	
Data Matrix barcode & RFID as enabler of the End-to-end	3,68	3,87	
Data Matrix barcode & RFID as enabler of the E-pedigree	3,84	4,00	

1: Mean based on Likert scales where 1 = not efficient and 5 = very efficient

2: Level of significance for the two-tailed t-test where * for p<0,10; ** for p<0,05; *** for p<0,01 and **** for p<0,001.

any of the *E-pedigree* system based on hybrid data carriers –i.e. *RFID* and *Data Matrix* (4,00): this last observation reinforces the notion that North Americans are indeed ambivalent about both data carriers and probably attempt to capitalize on the relative merits of each data carriers. For Europeans, *RFID as enabler of the End-to-end verification system* (4,00) represents a more effective technological solution but several respondents commented that the implementation of this solution would also be more complex and more expensive. A few respondents also indicated that counterfeiters would have more difficulties to circumvent *RFID* than *Data Matrix*, the later data carrier being easier to reproduce, and, that in the longer term, *RFID* will be proven to be superior.

C. The relative merits of Data Matrix barcode and RFID

Table III lists the relative merits of Data Matrix barcode and displays the mean value for Europe and North America. From the results displayed in Table III, the following can be observed:

- 1) Both Europeans and North-Americans consider that the *low cost* of Data Matrix represents the most important advantage (first rank, means equal to 4,58 and 4,32 respectively). The second most important advantage from both perspectives is the capacity of Data Matrix to be a *short-term workable solution* (4,39 vs. 4,24 respectively). Along the same lines, both regions also agree that Data Matrix is a *proven technology in several industries* and is *compatible with 1D barcode systems*. All these four advantages are related to a well-established technology.
- 2) Europe and North America differ significantly on the capacity of Data Matrix to be *marked directly on the package* which is considered as the third most important

by Europe (4,36), but it is rated as one of the less important advantage by North America (3,66).

3) Among the least important advantages, Europe and North America rank the ability of Data Matrix to *be recognizable by consumers* and *readable by humans*.

4) Europeans consider that the *line of sight required* by Data Matrix remains its most important drawback (3,71) while North Americans believe that its *easy reproduction* is definitely a shortcoming (4,06).

5) The inability of Data Matrix to bring *benefits in terms of logistics management* is significantly a more important drawback for Americans than for Europeans.

Do Europeans and North-American agree on the relative merits of RFID? Table IV offers some answers to that question.

From the results displayed in Table IV, the following can be observed:

- 1) For Europe, the three most important characteristics of RFID are the capacity of RFID technology to *add intelligence* of supply chain processes, (4,43), followed by the ability to *collect data in real time* (4,42) and the possibility to *share data between partners* (4,41). Surprisingly, and in sharp contrast, North-Americans view the capacity of RFID to increase the *accuracy for shipping and receiving* medicines as the most important advantage (4,33), followed by the ability to *make tough its reproduction* (4,27) and to *reduce thefts and product substitutions* (4,15).
- 2) In terms of drawbacks, the cost of RFID seems to be an overriding concern for all respondents. The *lack of common and established standard* (3,77) is rated as the least important drawback for Europeans while the North-Americans seem the particularly concerned by the *potential problems with liquid products* as the less important drawbacks (3,53).

TABLE III
 THE RELATIVE MERITS OF DATA MATRIX

	Europe (n=34)		North America (n=38)		
	Mean	Rank	Mean	Rank	
Advantages of Data Matrix					
Superior data capacity than 1D barcode	4,32	4	4,03	7	
Small size	4,23	8	3,84	12	
Robustness: error correction system	4,16	10	3,97	9	
Limited upgrades to work with current systems	3,97	14	3,87	11	
High accuracy and good read rates	4,26	7	4,05	6	
Direct marking on the package	4,36	3	3,66	15	**
Multi-directional reading	4,10	11	3,74	13	
Readability even with low contrasts	4,00	13	3,87	10	
Usable with current printing technologies	4,07	12	4,11	5	
Compatible infrastructure with 1D barcode systems	4,19	9	4,18	4	
Mass serialization	4,26	6	4,03	8	
Low cost technologies	4,58	1	4,32	1	
Short term workable solution	4,39	2	4,24	2	
Proven technology in various industries	4,29	5	4,21	3	
Recognizable by consumers	3,77	15	3,70	14	
Human readability	3,57	16	3,58	16	
Drawbacks of Data Matrix					
Line of sight required	3,71	1	3,68	3	
No benefits in term of logistic management	2,93	4	3,65	4	**
Easy to produce	3,58	2	4,06	1	
Item-by-item scanning, higher labor costs	3,55	3	4,03	2	

1: Mean based on Likert scales where 1 = not important and 5 = very important

2: Level of significance for the two-tailed t-test where * for p<0,10; ** for p<0,05; *** for p<0,01 and **** for p<0,001.

D. Discussion

Additional insight is gained by analysing the comments of participants from the on-site interviews and to the e-survey. The existing legislative framework appears inadequate (Table I) but several respondents commented that laws are “necessary.” One American respondent pointed that any technological strategy would remain inefficient without adequate legislation.

From these comments, we can also observe a consensus among participants for increasing the visibility of medicines through the supply chain and serialising them at the unit level since only the assignation of a unique and random serial to each unit could stop the penetration of counterfeit medicines in the different layers of the legal supply chain (Figure 3). However, a few respondents indicated that neither *End-to-end verification system* nor *E-pedigree system* could stop the (illegal) commercialisation of counterfeiting medicines on the Internet. The participants offer conflicting opinions about the effectiveness of each technological strategy. Europeans stress that *E-pedigree system* is “the most secure but its implementation is chaotic,” and it offers higher security levels but entails a high cost and logistic issues due to “the amount of data that must be segregated”. Some European respondents added that *E-pedigree system* could not be implemented because it’s difficult to establish control measures at each level of the supply chain whereas the *End-to-end verification system* is much easier to implement because it implies only

two points of control: at manufacturer level before medicines enter to the distribution chain and at retailer level before medicines are dispensed to the final consumers. One North American participant argued that “the *End-to-end verification system* cannot be implemented in North America because medicines are not dispensed in their original package.” Indeed, Canadian and American retail pharmacies dispense prescription medicines by pills in small plastic containers or bottles, which do not allow consumers to verify the authenticity of medicines. If retail pharmacies are “corrupted”, they could dispense counterfeit medicines. In order to ensure the security of consumers, stricter measures of control for retail pharmacies are needed.

For all respondents, *Data Matrix* could be used as a data carrier for both *End-to-end verification system* and *E-pedigree systems*. Europeans and North Americans favour this technology because of its low cost and because it could be implemented in the short term. This technology could be “easily implemented by the manufacturers and used at the retail level” since *Data Matrix* barcode can be directly marked on the package, it is a proven technology in various industries and it demonstrates high accuracy and good read rates. Europeans are less sensitive to the fact that *Data Matrix* does not generate some logistic benefits but appear to favour an easily implemented solution in order to ensure the security of consumers.

TABLE IV
THE RELATIVE MERITS OF RFID

	Europe (n=34)		North America (n=38)		
	Mean	Rank	Mean	Rank	
Advantages of RFID					
No line of sight required	4,21	6	4,00	8	
Multiple tag and multi-item reading	4,24	5	3,91	12	
Read and write capability	4,07	9	3,79	14	
Superior data capacity	4,00	10	3,70	16	
Data sharing between partner	4,41	3	3,94	9	*
Added intelligence	4,43	1	3,88	13	**
Real time data collection	4,42	2	4,06	6	
Difficult to reproduce	4,00	11	4,27	2	
Full track and trace	4,17	8	4,12	4	
Mass serialization	4,19	7	4,12	5	
Inventory control while keeping stocks visible	4,00	12	3,94	10	
Shipping/receiving accuracy	3,89	13	4,33	1	*
Product recall	3,82	14	4,00	7	
Expiration date management	3,72	15	3,94	11	
Reduction of material handling	3,46	16	3,76	15	
Reduction of thefts and products substitutions	4,24	4	4,15	3	
Drawbacks of RFID					
Lack of standards common and established	3,77	8	4,20	2	
Potential problems with liquid products	3,90	4	3,53	8	
Potential problems with accuracy of reading	3,87	6	3,69	5	
Concern about ownership of data	4,13	3	3,64	6	**
Conflicting issues about implementing responsibilities	4,23	2	3,81	4	*
Privacy concerns	3,80	5	3,61	7	**
Costs	4,60	1	4,22	1	*
Popularity of barcodes	3,87	7	3,83	3	

1: Mean based on Likert scales where 1 = not important and 5 = very important,

2: Level of significance for the two-tailed t-test where * for $p < 0,10$; ** for $p < 0,05$; *** for $p < 0,01$ and **** for $p < 0,001$.

In contrast, North Americans believe that *RFID* is an effective data carrier to ensure the identification of medicines and that it provides operational and logistic advantages for the pharmaceutical supply chain management. For instance, *RFID* allows to have an automatic control of medicines at any point of the supply chain in order to stop the injection of counterfeit medicines, and also to stop thefts and product substitutions. Europeans argue that *RFID* technology could bring operational and cooperative advantages to the pharmaceutical supply chain players. This technology permits to collect data in real time during the medicines distribution. This information could be used to automate operations and could be shared between partners in order to improve supply chain management. Both regions agree with the capacity of this technology to secure the supply chain but consider its high cost as a critical issue. Indeed, *RFID* implementation implies that all suppliers invest into an improved technological infrastructure relying in tags, readers, middleware and IT systems to reach and the central data base.

Hybrids solutions relying on both *RFID* and *Data Matrix* that could capitalize on the respective potential of the two data carriers are mostly favoured by North Americans, especially for the *E-pedigree system*. As one American participant indicated, «most are planning to use *RFID* at case level and use inference to assign events to 2D barcode items within the case » and observed that the relatively higher costs of *RFID*

technology decrease because only pallets and cases are tagged with *RFID*.

V. CONCLUSION

The magnitude, scope and impacts of counterfeit medicines necessitate the elaboration, adoption and implementation of effective technological strategies. However, our collective understanding of these strategies remains rather scarce. This paper represents an attempt to provide empirical evidence on the effectiveness of the two anti-counterfeiting strategies, namely the End-to-end verification system and the E-pedigree system and the associated data carriers, i.e. *Data Matrix* and *RFID*. Because counterfeit medicines are becoming a rising and widespread international concern, it is critical to better understand the respective positions of Europe and North-America, the two regions that are actively pursuing and deploying anti-counterfeit strategies. This paper therefore analyses the data provided from seventy two (72) key pharmaceutical supply chains actors who are located in Europe and North-America.

The results presented in this paper offer some valuable insights for top managers in pharmaceutical supply chains and IT specialists responsible for the implementation of the technological strategies. First, the consensus between Europeans and North-Americans is evident for several key issues: a) the current legislative system for fighting

counterfeiting activities is rather inadequate and stricter legislation remains necessary even with the deployment of effective technological strategies; b) mass serialization is indispensable for a robust information infrastructure; c) Data Matrix remains a well proven low cost technology while RFID offers high potential technology. Second, the several divergences, especially when assessing the relative merits of Data Matrix and RFID, run deep between the two regions. There is yet no evidence of a dominant design but the increased globalization of both the pharmaceutical chains and the counterfeiting activities does require the emergence of such a dominant design for a more coherent and more harmonized approach. Collaboration between all stakeholders of the pharmaceutical supply chains, including associations, governments, agencies and IT suppliers is therefore required for dealing effectively with the problem of counterfeit medicines. Third, managers and IT specialists associated to either the End-to-end verification system or the E-pedigree system may underestimate the resilience of the old technology (here Data Matrix) and overestimate the potential of new technology (RFID). A better appreciation of these issues, including the resistance to change, could offset future implementation problems.

The paper highlights the dynamics of the “interregnum” between the barcode technology and RFID. For technologists and IT experts, it is rather puzzling to conclude that the “best” or “superior” technology may very well not be chosen. Rather, the retained technological strategy for dealing with counterfeit pharmaceutical products will arise from the negotiated logic of all stakeholders.

APPENDIX 1

THEORETICAL JUSTIFICATION OF THE RELATIVE MERITS OF DATA MATRIX AND RFID

Advantages of Data Matrix barcode	
Superior data capacity than 1D barcode	[32]
Small size	[10], [32]
Robustness: error correction system	[10], [33]
Limited upgrades to work with current systems	[34]
High accuracy and good read rates	[10], [33]
Direct marking on the package	[35]
Multi-directional reading	[35]
Readability even with low contrasts	[35]
Usable with current printing technologies	[35]
Compatible infrastructure with 1D barcode systems	[34]
Mass serialization	[32]
Low cost technologies	[36], [37], [32], [55]
Short term workable solution	[10], [32]
Proven technology in various industries	[10], [37]
Recognizable by consumers	Adapted from [38]
Human readability	[32], [55]
Drawbacks of Data Matrix barcode	
Line of sight required	[10], [40], [42]
No benefits in term of logistic management	[10]
Easy to produce	[10], [40]

Advantages of RFID	
Item-by-item scanning, higher labour costs	[41], [33], [54]
No line of sight required	[36], [37], [39], [54], [55]
Multiple tag and multi-item reading	[37], [39], [43], [54]
Read and write capability	[39], [55]
Superior data capacity	[39], [54], [55]
Data sharing between partner	[39], [43]
Added intelligence	[39], [43]
Real time data collection	[6], [39], [44]
Difficult to reproduce	[45]
Full track and trace	[41], [46]
Mass serialization	[41], [40]
Inventory control while keeping stocks visible	[37], [43], [47], [53]
Shipping/receiving accuracy	[36], [48]
Product recall	[46]
Expiration date management	[46]
Reduction of material handling	[49], [43], [47]
Reduction of thefts and products substitutions	[49], [53]
Drawbacks of RFID	
Lack of standards common and established	[49], [50], [44]
Potential problems with liquid products	[34], [49]
Potential problems with accuracy of reading	[10], [33]
Concern about ownership of data	[49], [44]
Conflicting issues about implementing responsibilities	[33]
Privacy concerns	[49], [51], [54]
Costs	[36], [37], [52], [53], [55]
Popularity of barcodes	[43]

REFERENCES

- [1] C. I. Chen, Y. Y. Chen, Y. C. Huang, C. S. Liu, C. I. Lin and T. F. Shih, “Anti-counterfeit ownership transfer protocol for low cost RFID system,” *WSEAS Transactions on communications*, vol. 7, no. 8, pp. 1149–1158, Aug. 2008
- [2] WHO, “Counterfeit medicines: WHO,” Obtained through the WHO website, published on 2005. Available: http://www.wpro.who.int/health_topics/counterfeit_medicines/
- [3] J. A. Smith, “E-pedigree: an inevitability for the industry,” in *Pharmacy times*, published on April 1, 2009. Available: <http://www.pharmacytimes.com/issue/pharmacy/2009/2009-04/2009-04-10229>
- [4] WHO, “Medicines: counterfeit medicines,” obtained through the WHO website, published in 2010. Available: <http://www.who.int/mediacentre/factsheets/fs275/en/>
- [5] M. S. Matalka, J. K. Visich and L. Suhong, “Reviewing the drivers and challenges in RFID implementation in the pharmaceutical supply chain,” *International Journal of Electronic Business*, Vol. 7, pp. 473-490, 2009
- [6] E. Schuster, S. Allen and D. Brock, “Global RFID: the value of the EPCglobal network for supply chain management” New York: Springer Verlag, 2007
- [7] R. Jameson, J. Chin, F. Peo, L. Gonzales and D. Lorence, “Using IP law as a medical patient safety tool: efforts from the US and China,” *International Journal of Intellectual Property Management*, Vol. 3, pp. 155-168, 2009.
- [8] N. Basta, “Product Security Perspective: Protecting the Brand, Pharmaceutical Commerce” Obtained through the *Pharmaceutical Commerce website*, published in 2009. Available: http://www.pharmaceuticalcommerce.com/frontEnd/991-serialization_antcounterfeiting_pedigree_RFID_taggants_barcode.html

- [9] V. Leopoulos, K. Kirytopoulos and D. Vouldaridou, "Electronic alliances and the (para)pharmaceutical supply chain: Identification of risks," in Proc. *WSEAS International conference on dynamical system and control*, Venice, Italy, November 2005, pp. 247-252.
- [10] J. Bobée, "How technology can help to fight counterfeits? Apport de la technologie dans la lutte contre la contrefaçon de médicaments," *STP Pharma pratiques*, Vol. 19, pp.29-40, 2009
- [11] EFPIA, "Towards safer medicines supply, Business case. Brussels: European Federation of Pharmaceutical Industries and Associations," Business case, Version 4.0, January 2008, Brussels, 21 p.
- [12] Y. Uchida, S. Matsuno and T. Tamaki, "Development of a traceability system based on open source software for small, and medium enterprises in Japan," in Proc. *3rd WSEAS International conference on computer engineering and applications*, CEA, 2009
- [13] N. A. Anir, N. M. H., Nizam, A. Masliyana, "The users perceptions and opportunities in Malaysia in introducing RFID system for Halal food tracking," *WSEAS Transactions on information science and applications*. Vol. 5, no. 5, May 2008, pp. 843-852
- [14] L. C. G. Budacia, E. A., Budacia and I. Iacob, "Identification based on radio frequency (RFID) – a new information technology with broad applications in economics," in Proc. *10th WSEAS International conference on mathematics and computers in business and economics*, Prague, Czech Republic, 2009, pp. 94-99.
- [15] S. Srinivasan, A. Aggarwal and A. Kumar, "RFID Security and privacy concerns," in Proc. *4th WSEAS International Conference on Information Security*, Communications and Computers, Tenerife, Spain, December 2005, pp. 69-74.
- [16] R. S. Chen, C. C. Chen, K. C. Yeh, Y. C. Chen and C. W. Kuo, "Using RFID technology in food produce traceability," *WSEAS Transactions on information science and applications*, Vol. 5, No. 11, November 2008, pp. 1151-1160.
- [17] C. L. Lai, S. W. Chien, S. C. Chen and K. Fang, "Enhancing medication safety and reduce adverse drug events on impatient medication administration using RFID," *WSEAS transactions on communications*, Vol. 7, No. 11, October 2008, pp. 1045-1054.
- [18] R. M. Henderson, "Of Life Cycles Real and Imaginary: The Unexpectedly Long Old Age of Optical Lithography," *Research Policy*, Vol. 24 No. 4, 1995, pp. 631-643.
- [19] S. M. Ansari, R. Garud, "Inter-Generational Transitions in Socio-Technical Systems: The Case of Mobile Communications," *Research Policy*, Vol. 38, No. 2, 2009, PP. 382-392.
- [20] R. Want, "RFID: A key to Automating Every Thing" *Scientific American*, Vol. 290, 2004, pp. 56-65.
- [21] C. Chao, J. Yang and W. Jen, "Determining technology trends and forecasts of RFID by a historical review and bibliometric analysis from 1991 to 2005" *Technovation*, Vol. 27, No. 5, 2007, pp. 268-279.
- [22] B. Srivastava, "Radio frequency ID technology: The next revolution in SCM", *Business Horizons*, vol. 47, No. 6, 2004, pp. 60-68
- [23] Y. Sheffi, "RFID and the innovation Cycle", *Int. J. og Logistics Management*, Vol. 15, No. 1, 2004, pp. 1-10.
- [24] C. Heinrich, "RFID and Beyond" Wiley, Indianapolis (2005).
- [25] B. Arthur, "Competing Technologies: An Overview" In: Dosi, G., (Ed.) *Technical Change and Economic Theory*, New York: Columbia University Press, 1987.
- [26] M. L. Markus, "Toward a 'Critical Mass' Theory of Interactive Media: Universal Access, Interdependence and Diffusion." *Communications Research*, Vol. 14, 1987, pp. 491-511.
- [27] OECD, "The economic impact of counterfeiting and piracy: OECD," Paris: OECD publishing, 2008.
- [28] HSC, "Follow the pill, understanding the U.S. commercial pharmaceutical supply chain: Kaiser Family Foundation" White paper, March 2005, 32 pages.
- [29] J. Gallagher and J. Colaizzi, "Issues in Internet pharmacy practice". *The Annals of Pharmacotherapy*, Vol 34, No. 12, 2000, pp.1483.
- [30] A. Peterson, "A survey of selected Internet pharmacies in the United States". *Journal of American Pharmaceutical Association*, Vol. 41, No. 2, 2005, pp. 205-212.
- [31] EAASM, "The Counterfeiting Superhighway". Published in 2008. Obtained through the Internet. Available: http://v35.pixelcms.com/ams/assets/312296678531/455_EAASM_count erfeiting_report_020608.pdf
- [32] J. Rittenburg, "Follow-up comments to the April 13, 2007", *IMPACT technology review held in Prague, Czech Republic: IMPACT*, 2007.
- [33] M. Potdar, E. Chang and V. Potdar, "Applications of RFID in pharmaceutical industry" Presented at *IEEE International Conference on Industrial Technology*, December 2006, (pp. 2860-2865).
- [34] S. Dahod, and L.T. Kontnik, "Safe and Secure". in *PharmExec.com*, Septembre 1, 2004
- [35] GS1 France, "Data Matrix ECC200, changer de dimension avec le GS1 Data Matrix ECC200".
- [36] M. Aichlmayr, "Bitter Pill". Published in *Material Handling Management in 2007*, http://mhmonline.com/facilities-management/mhm_imp_5819/S
- [37] K. Brooks, "Anti-Counterfeiting Initiatives and RFID Practices". *Contract Pharma*, January/February 2006.
- [38] A. K. Deisingh, "Pharmaceutical Counterfeiting" *The Royal Society of Chemistry 2005, Analyst 2005*, Vol. 130, pp. 271-279.
- [39] E. Lefebvre, Y. Bendavid, L.A. Lefebvre, "Open innovation strategies in shaping technological progress: the case of RFID" *The Third European Conference on Management Technology (EUROMOT)*, 2008, Nice, France.
- [40] N. Howe, S. Goldner and C. Fenning, C. "Drug Pedigrees: Your Supply Chain Needs Them: Are You Ready?" *Pharmaceutical Engineering*, Vol. 27, No. 6, 2007.
- [41] HDMA, "Protecting Safety and Improving Efficiencies in the Health Care Supply Chain - Using Electronic Product Codes", 2003.
- [42] M. Roberti, "Pharma Pounders a Track-and-Trace System" Published in *RFID Journal*, Nov, 24, 2008. Consulted from: <http://www.rfidjournal.com/article/articleview/4465/1/2/>
- [43] M. Tajima, "Strategic value of RFID in supply chain management", *Journal of Purchasing & Supply Chain Management*, Vol. 13, 2007, pp. 261-273.
- [44] A. White, M. Johnson and H. Wilson, "RFID in the supply chain: lessons from the European early adopters" *International Journal of Physical Distribution & Logistics Management*, Vol. 38, No. 2, 2008, pp. 88-107.
- [45] I. Chakrabarti, "An Auto-ID Based Approach to Reduce Counterfeiting in the U.S Pharmaceutical Supply Chain" in Master of Science, Massachusetts Institute Technology, 2003. Consulted from: <http://dspace.mit.edu/bitstream/handle/1/721.1/28568/57456391.pdf?sequence=1>
- [46] D. Sujovit, "Track 'n' trace: securing the drug supply chain", from Cognizant's RFID Center of Excellence, discusses the drug supply chain. *Pharma*, 1st july 2009.
- [47] B. Kelly, "Securing the Drug Supply from Counterfeiting Protects Brand Profits". *Pharmaceutical Manufacturing and Packaging Sourcer*, Winter 2004.
- [48] M. Attaran, "RFID: an enabler of supply chain operations". *Supply Chain Management: An International Journal*, Vol. 12, No. 4, 2007, pp. 249-257.
- [49] FDA, "FDA Counterfeit Drug Task Force Report: 2006 Update" in FDA, 2006.
- [50] S.A. Murphy, "Logistics technology: Pfizer places an accent on security". *Logistics Management*, 18 February 2009.
- [51] M. Hayes Weier, "Two Years IN, RFID's Not The CURE". In *Information Week*, 20 november 2006.
- [52] S. Fosso Wamba, B. Keating, T. Coltman, and M. Katina, "RFID Adoption Issues - Analysis of Organizational Benefits & Risks" May 2009.
- [53] V. Pormieks and E. Glinters, "RFID Protocol Evaluation Using Bayesian Networks". *Proceedings of the 11th WSEAS International Conference on Automatic Control, Modelling and Simulation*, 2008
- [54] V. Pormieks and E. Glinters, "Security problems of RFID authentication protocols". *Proceedings of the 6th WSEAS International Conference on System Science and Simulation in Engineering*, Venice, Italy, November 2007.
- [55] E. Lutton, B. Regan and G. Skinner. "The role of Radio Frequency Identification and Bar code technologies" *Journal of Mathematical Methods and applied computing*, 2009, pp:164-169
- [56] R. S. Chen, C. C. Chen, K. C. Yeh, Y. C. Chen and C. W. Kuo, "Using RFID technology in produce traceability," In *Proceedings of the 10th WSEAS international conference on mathematical methods, computation techniques and intelligent systems*, 2008, pp:421-425.