Assessing the relative effectiveness of technological strategies for fighting counterfeit medicines

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

Abstract—One tenth of the medicines commercialized around the world are counterfeit medicines, representing an estimated value of 75 billion US dollars in 2010 and raising serious security and health concerns. This paper focuses on the technological initiatives undertaken by the stakeholders of different pharmaceutical supply chains. More specifically, we will analyze the two overall technological strategies, namely the end-to-end verification system vs. E-pedigree system, and the two competing technologies which are envisioned to act as data carriers, the two-dimensional barcode called Datamatrix, 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.

Keywords—Counterfeit medicines, Pharmaceutical supply chain, the End-to-end verification system, E-pedigree system, 2D barcode Datamatrix, 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 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 anticoagulant 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 Datamatrix, 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 have been 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 primary and secondary package is ensured by tamper-evident in the supply chain then record the financial transactions and warnings or advisory notices [11]. As manufacturers and retailers must have access to the 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 2D barcode Datamatrix 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 Datamatrix, more specifically the 2D Datamatrix ECC200 [11]. Datamatrix (left hand side 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 [11]. This barcode can carry an important amount of data on a small space, 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] 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 side of Figure 2). The RFID tag transmits this data directly and without direct line of sight to a reader by radio frequency [14]. 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] and holds the potential to improve logistical operations [16], [13]. 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.

![Fig. 2 The respective infrastructure for the two data carriers (Datamatrix barcode vs. RFID)](image)

C. Datamatrix 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 Datamatrix. In the greater Stockholm area, 110,000 units were recorded with Datamatrix 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 Datamatrix and RFID. For example, cases and pallets can be tracked with RFID tags, while medicines can be with Datamatrix. 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 Datamatrix, 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 on 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 (pharma 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 3) 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 counterfeit, 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].

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 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 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

In order to compare the position of European organizations to the one held by North-American organizations, bilateral t-tests were conducted on the effectiveness of the envisioned technological strategies. Qualitative data based on the comments of the respondents is also examined and contrasted with the quantitative data. 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 1 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.

<table>
<thead>
<tr>
<th>Effectiveness of different technological strategies</th>
<th>Europe (n=34)</th>
<th>North America (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall technological strategies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-pedigree – track &amp; trace system effectiveness</td>
<td>3.84</td>
<td>3.46</td>
</tr>
<tr>
<td>End-to-end verification system effectiveness</td>
<td>4.03</td>
<td>3.29 ***</td>
</tr>
<tr>
<td><strong>Data carriers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RFID effectiveness</td>
<td>3.75</td>
<td>3.34</td>
</tr>
<tr>
<td>Datamatrix barcode effectiveness</td>
<td>4.00</td>
<td>3.32 ***</td>
</tr>
<tr>
<td><strong>Combining the two systems with the two data carriers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RFID as enabler of the E-pedigree</td>
<td>3.97</td>
<td>3.97</td>
</tr>
<tr>
<td>RFID as enabler of the End-to-end verification system</td>
<td>4.00</td>
<td>3.68</td>
</tr>
<tr>
<td>Datamatrix barcode as enabler of the E-pedigree</td>
<td>3.69</td>
<td>3.73</td>
</tr>
<tr>
<td>Datamatrix barcode as enabler of the End-to-end</td>
<td>3.81</td>
<td>3.68</td>
</tr>
<tr>
<td>RFID &amp; Datamatrix barcode as enabler of the E-pedigree</td>
<td>3.84</td>
<td>4.00</td>
</tr>
<tr>
<td>RFID &amp; Datamatrix barcode as enabler of the End-to-end</td>
<td>3.68</td>
<td>3.87</td>
</tr>
</tbody>
</table>

1: Mean based on a Likert scale 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.

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

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. 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 postenonements such as the of 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).

2) Europeans rate significantly **Datamatrix** as a more effective data carrier for mass serialisation than **RFID**, while North Americans remain ambivalent about both data carriers as it can be deduced from the very similar means (3.32 and 3.34).

3) Of all possible combinations between the two systems and the two data carriers, North Americans tend to prefer any of the **E-pedigree system** based on hybrid data carriers –i.e. **RFID** and **Datamatrix** (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 **Datamatrix**, the later data carrier being easier to reproduce. And that in the longer term **RFID** will be proven to be superior.

Additional insight is gained by analysing the comments of participants to the on-site interviews and to the e-survey. From these comments, we can 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 counterfeit 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 the 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 does 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.

European and North American respondents argue that **Datamatrix** could be used as data carrier for both **End-to-end verification system** and **E-pedigree system**. However, most North American seems to favour hybrids solutions, relying on both **RFID** and **Datamatrix**, 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

Counterfeiting medicines is a high profit margin activity [6] with low production costs [32] and rather low risks of detection. Counterfeiters can easily imitate medicine labels and packages [6] since advancements in software and hardware allow improving the quality of imitations. Consumers and even supply chain players cannot distinguish between the copy and the genuine package [10]. Existing regulations against counterfeiters are not strict enough [27].
and counterfeiting activities and unauthorized distributions are not severely persecuted in some countries [6]. Counterfeit medicines can easily enter in the pharmaceutical supply chains due to their inherent characteristics, namely their complexity, the abundance of players selling and distributing medicines, and the increasing variety of products. [33], [6]. Each time medicines move from one player to the next, counterfeit products can be injected. In order to circumvent the counterfeiting problem, different technological strategies relying on either the End-to-end verification system or the E-pedigree system and using Datamatrix or RFID or both data carriers are foreseen by main actors in pharmaceutical supply chain in Europe and North America. However, the adoption of these technological strategies remains difficult, complex and expensive and no consensus has yet emerged.

Of all the technological strategies that are sought, there is no guarantee that the “best” technological solution for fighting counterfeit medicines will be chosen. Instead, the retained technological strategy will emerge from the negotiated logic of all stakeholders involved in different pharmaceutical supply chains. The increased globalization of pharmaceutical supply chains will however require a coherent and harmonized worldwide approach to effectively combat counterfeiting.

REFERENCES