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European Federation of Pharmaceutical Industries and Associations

Apoteket AB

EFPIA Product Verification Project

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Foreword

One of the pharmaceutical industry's principal concerns is to ensure patient safety. We want to be confident that the patient receives the genuine medicine that has been prescribed. The growing threat to the integrity of the supply chain over recent times is a significant concern and I am very pleased that our industry has taken proactive steps to address this important issue.

The application of modern technology enables us to introduce a verification system across the European Union. The system piloted by EFPIA and Apoteket AB in Sweden has demonstrated the feasibility and effectiveness of a unique coding system and point of dispensing verification, which can and will contribute to enhancing patient safety.

This initiative represents an important contribution to meeting the challenge posed by counterfeit medicines entering the legitimate supply chain. By investing in this pilot project, the research-based pharmaceutical industry has demonstrated its ongoing commitment to patient safety.

I am delighted with the results of the pilot and I commend the report.

London - April 2010

David Brennan
CEO Astra Zeneca

The participation of Apoteket AB in the EFPIA Product Verification Pilot in Sweden has been successful. During a period of extensive changes going on in the Swedish retail pharmacy market we have been able to participate in this study in order to contribute to increased safety in the supply of medicines to the public. Apoteket has learned a lot from the participation in the study. The model with 2-D matrix codes seems to be useful both for the purpose of preventing counterfeit medicines as well as for other management purposes in the pharmacies.

We also hope that the results and the experiences of this pilot study will contribute to the development of further patient safety in Sweden as well as in other parts of the world.

This project has been a very good example of a close and constructive co-operation between the pharmaceutical industry, the wholesalers, the authorities involved and the retail pharmacy chain.

In the new competitive retail pharmacy market in Sweden, we do look forward to other such well-functioning cooperation projects in the name of better patient safety and development of pharmacy management.

Stockholm - April 2010

Stefan Carlsson
CEO Apoteket AB

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Acknowledgements

From the beginning, the concept proposed by EFPIA was based on the idea of cooperation between the different stakeholders in the pharmaceutical supply chain. Ensuring patient safety by implementing a system that involves the participation of several stakeholders must not only be based on a set of rules but also the willingness and ability to cooperate. EFPIA would therefore like to express its appreciation to all the project partners who have voluntarily contributed to this project in a genuine spirit of cooperation, which has been instrumental to the success and rapid development of this project.

This includes first and foremost, the Swedish pharmacy retailer *Apoteket AB* at both management level (i.e. Lars Rönnbäck and Birgitta Lange-Sjöblöm) as well as at operational level with special thanks to Petra Öström and all the participating pharmacists involved in the project. The support of Swedish pharmaceutical manufacturers' association ("Läkemedelsindustriföreningen", Lif) but also Swedish wholesalers *Tamro AB* and *KD Pharma AB* who have also actively contributed by facilitating the labelling and distribution of packs.

One should not ignore the level of political alignment necessary both internally within the industry and externally in developing the framework for this project. Credits for this go to the project chairs Jean-Marc Bobée (Sanofi Aventis) and Andrew Bonser (Pfizer) whose activism has been essential in communicating the industry objective externally but also to ensure support of industry executives for this project. This was also ensured by the active support of project champion David Brennan (CEO Astra Zeneca) and former EFPIA president Arthur Higgins (CEO Bayer HealthCare) who ensured the necessary resources to support the development of this project.

Finally, EFPIA would also like to thank all the experts from its member companies involved in both the technical and operational developments of this project. These include the heavy work involved in preparing the user requirement specifications, reviewing and selecting the IT solution providers as well as managing the logistic aspects of the project both in Brussels and in Sweden. All this was professionally managed and coordinated by EFPIA Project Manager Martin Friedrich (Bayer Technology Services), but also external experts and consultants Paul Mills (Melior Solutions Ltd) and Marianne Rönnbäck (Litoda AB).

Executive Summary

In September 2009, EFPIA in collaboration with pharmaceutical retail chain Apoteket AB launched a coding pilot project, testing a pharmacy-based verification system using a 2D Data Matrix code (DMC) on each medicine pack dispensed. The project was carried out in cooperation with the Swedish pharmaceutical manufacturers' association ("Läkemedelsindustriföreningen", Lif) and the support of the pharmaceutical distributors Tamro AB and KD Pharma AB.

The pilot was run for approximately four months in 25 pharmacies, during which period more than 95,000 packs were scanned and verified before they were dispensed. The packs used in the project had been supplied by 14 leading pharmaceutical companies.

EFPIA undertook the project to demonstrate the feasibility and effectiveness of its approach to enhance patient safety and supply chain security, known as "Product Verification at the Point of Dispense". This can be seen as a response to the European Commission's Draft Directive on counterfeiting, aimed at reducing the risks of counterfeit medicines entering the legitimate supply chain. To protect public health and eliminate counterfeits means putting in place a comprehensive series of measures. These include harmonised product serialisation, the universal use of safety features, the integrity of the pack throughout its lifetime and the dispense of the original pack.

Apoteket undertook the project in order to contribute to the development of a new system that could improve patient safety. In addition to this, the 2D-matrix code was an important characteristic to test in order to evaluate against the current coding system in Sweden, which for several reasons needs to be changed. The 2D matrix code, which can carry more information than an ordinary bar code is therefore a coding system that could provide pharmacies with additional advantages for stock management (batch control, withdrawals, expiry-date control etc.)

A product verification system at the point of dispense (i.e. Pharmacy or Hospital) offers good scope for improving both supply chain security and patient safety. Paramount is that the system is harmonized and interoperable across Europe. If the safe and free movement of medicines across borders is to be improved, a coordinated approach to identification and verification of medicines is essential. EFPIA believes this requires all national coding systems to be interoperable and based on common standards.

This way, any pharmacist in any country can verify whether a pack with the same serial number has been dispensed before, independent of its country of origin. Accredited full-line wholesalers would also be able to have the option to access the database to check the status of the product at any time if in doubt, either before sending a product to the pharmacists or upon return of the product by the pharmacists. Without standardization and interoperability, there is a risk that the national identification and verification systems will be fragmented, limiting the ability to verify a product's

provenance to national product codes. This would present the problem of identifying counterfeit products crossing borders.

Furthermore, the solution needs to both garner the support of all stakeholders, which means effectively addressing their needs. Imposing high-end or expensive solutions throughout the supply chain is likely to generate resistance.

The results of the project were analysed by measuring key technical elements, such as system availability, reliability, and performance, by collecting and reviewing user feedback as well as by external assessment of IT system security and protection of data.

Key results of the pilot study show that:

- The model works in practice.
- The system allows for effective identification of fake packs as well as expired or short dated packs and recalled products.
- Availability and performance allow pharmacists to work at normal pace and without significant additional effort.
- The system is easy to use when fully integrated into the pharmacy workflow and existing pharmacy Point of Sales system.
- The two previous aspects lead to very high user acceptance.

Other learnings of the pilot project

- In order to achieve sustained credibility, the system must provide the correct answer to all transaction requests.
- The system should be customised to the existing pharmacy workflow as well as local conditions and regulatory requirements.
- The presence of more than one code on the pack causes confusion for the user and will jeopardise user acceptance.
- The necessary data segregation and data security can be technically ensured.
- Pharmacists are interested to get expiry date and batch number in machine-readable form.

1 Introduction

The need to ensure the safety and security of the supply chains has become a growing concern for industry and pharmacists alike. The risk of counterfeit medicines infiltrating the legitimate supply chain has become greater than ever before and has begun to raise concerns over the capabilities of the current supply chain system to cope with more sophisticated and organised criminal activities. In addition, the ongoing need to develop ever more efficient product surveillance systems that reduce the risks linked to product dispensing has lead to the conclusion that some traceability improvements are currently needed in the pharmaceutical supply chain.

EFPIA and Apoteket set itself the objective of implementing a pilot project in order to demonstrate the feasibility of the system described above, allowing for the verification of individual pharmaceutical products at the point of dispensing. This involved the following objectives:

1. Testing the technical capabilities of the system and ensure that the system as currently designed can be integrated into existing user operations (manufacturers, wholesalers, pharmacists).

2. Developing a model that benefits all stakeholders and ensures that conditions required for support of all partners are met.

The pilot project was therefore aimed at testing and demonstrating the following

- To develop and install a standardised national product verification system for use, initially with prescription based medicines,
- To demonstrate that a system could be made secure in terms of threat from both 'external' forces and 'internal' subversion.
- To provide a suitable and secure means for the pharmacy operation and operative to interface simply with the verification system in a manner that least impacts the standard means of dispensing product.
- To provide an efficient mechanism to maximise the ability to prevent recalled product from reaching the patient and aid the development of more effective recall processes within the supply chain.
- To develop and install, for use during 2009, a pilot system capable of undertaking selected functions of the full system with a significantly lower volume of product data.
- To provide an efficient means by which product usage data can be extracted and used by the system stakeholders.

2 The Approach for Product Verification at the Point of Dispense

2.1 Overview

The approach to product verification suggested by EFPIA is based on the premise that each pharmaceutical package is checked individually before it is dispensed to the patient. The system to achieve this goal consists of two main components:

1. The manufacturer of a pharmaceutical product applies a machine readable unique code to each individual sales pack and transmits the code content to a central data base prior to releasing the product to the market.

2. The pharmacist verifies each pack before it is dispensed to the patient by scanning the code and having its content compared to the information stored in the central database. The pharmacist is immediately informed about the result. As soon as the pack is sold its status in the database will be changed to "dispensed".

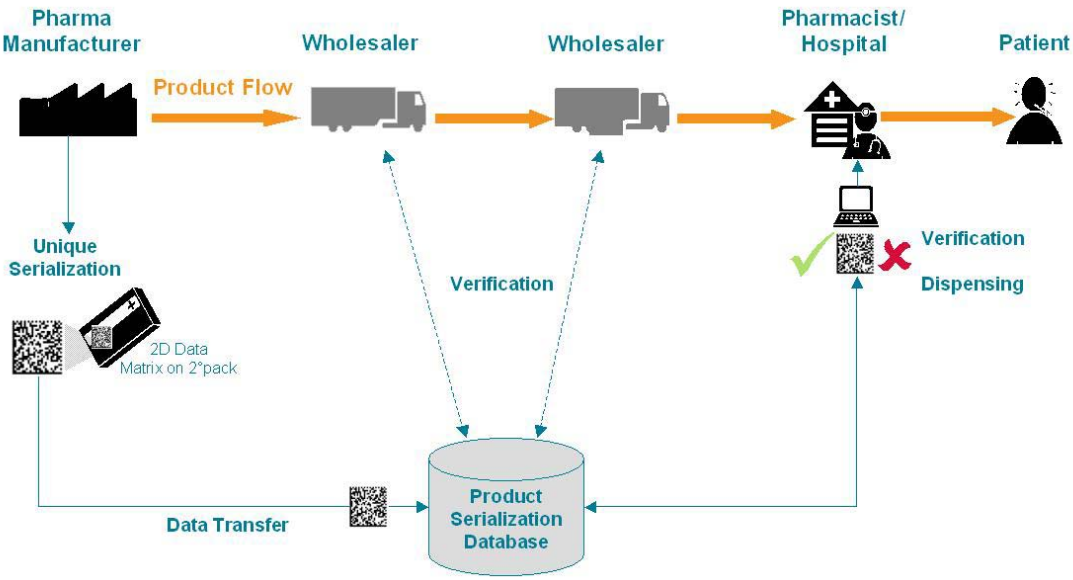

Figure 1 - EFPIA Product and Verification System: Product and data flow

A graphical representation of the related product and data flow is shown in Figure 1. While the verification of each pack is mandatory before it is sold, there is also the option to scan the pack at other locations (e.g. wholesalers) in the supply chain to verify its state. It should be noted, however, that data traffic must be managed to ensure sustained high performance and the risk for attacks on the host system must be minimised. These are important reasons to grant access to the central database only to authorised users using a secure connection.

2.2 Content and Format of Data Matrix Code

The suggested code is a Data Matrix code and contains four elements of information, i.e. article number, batch number, expiry date and a randomised serial number. The combination of article and serial number provides the pack's unique identity. The exact form of the information included in the Data Matrix code follows the GS1 Data Matrix standard and is described in the EFPIA "European Pack Coding Guidelines" [1]. An example of a DMC is given in Figure 2.

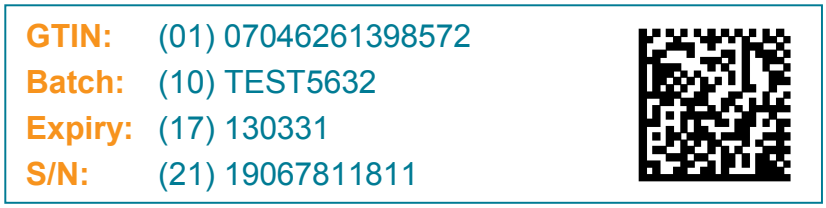

Figure 2 - Example of a Data Matrix Code with encoded information

Furthermore, the document provides suggestions regarding both the size and the quality of the Data Matrix code and with respect to the human readable representation of its contents on the sales pack. Finally, the guideline formulates criteria on the degree of randomisation for the serial numbers to avoid that they can be easily guessed by a counterfeiter. A set of basic tests verifying that the randomisation criteria are fulfilled for a given set of serial numbers has been provided through an Excel based randomisation test bed [2].

3 The Pilot Project

3.1 Overview

EFPIA in collaboration with Apoteket AB conducted a pilot project in order to demonstrate the feasibility of the proposed approach to product verification. The pilot was carried out in Sweden during the period of 17 September 2009 to 25 January 2010 in cooperation with the Swedish pharmaceutical manufacturers' association ("Läkemedelsindustriföreningen", Lif). Apoteket selected 25 pharmacies in the greater Stockholm area to participate in the project (cf Figure 3). The total number of dispensing points in the selected pharmacies is about 180 while the number of dispensing points per pharmacy ranges from 2 to 10.

Fourteen pharmaceutical companies provided a total of 25 products for participation in the pilot. Section 3.2 provides a list of manufacturers who contributed some of their products to the project. It was the goal of EFPIA to have about 100,000 packs verified and dispensed during the duration of the operational phase of the pilot. The number of packs to be coded per product was determined based on the sales forecast for the targeted four-month period.

Figure 3 - Swedish region with Pharmacies participating in the EFPIA pilot

All participating pharmacies were equipped with new scanners capable of reading Data Matrix codes to allow for product verification. Also, the existing Point of Sale (POS) software was amended to include the necessary extra functionality. Product verification and dispense operations were fully integrated into the ordinary pharmacy workflow. More details on the work process and the respective SW changes are provided in section 3.3.2.1.

The following sections provide a description of all of the project's relevant activities, starting with the description of product supply for the pilot, followed by presentations of the necessary information and communication system as well as preparation of the operational phase and project results.

3.2 Product Supply

The following fourteen EFPIA member companies provided 25 different products to be coded for the pilot project.

1. Amgen
2. Astra-Zeneca
3. Bayer HealthCare
4. Boehringer Ingelheim
5. GlaxoSmithKline
6. Janssen Cilag
7. Lundbeck
8. Merck Serono
9. Novartis
10. Novo Nordisk
11. Nycomed
12. Pfizer
13. Roche
14. Sanofi Aventis

About 112,000 packs were coded. This is an excess of about 10 % compared to the target number of packs to be verified and dispensed during the pilot operational phase. The reason to plan for some excess packs was an expected "loss" during start up and phase out of the pilot due to coded packs not being scanned during these phases.

3.2.1 Pack coding and registration

Packs coded were plastic bottles and folding boxes. The Data Matrix codes (DMC) were applied to the packs using self-adhesive labels on which the DMC was printed using thermal transfer printers. The pack's serial number is displayed next to the DMC in human readable form (see Figure 4).[1]

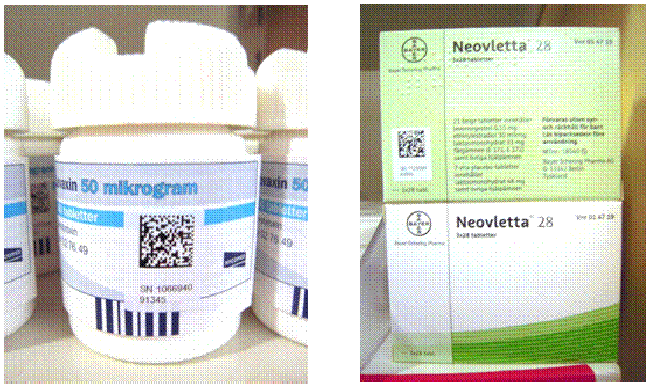

Figure 4 - Examples of Coded Packs

Coding products required approval of the Swedish "Medical Products Agency" (MPA). All manufacturers filed applications for labelling of their respective products and received approval before the labels were affixed to the packs.

Labelling was performed by the established distributors in the Swedish pharmacy supply chain, Tamro AB and KD Pharma AB.

[1] It should be noted that coding packs using labels is not the generally preferred way. It has been used for the very limited number of packs used in the pilot. For a large scale system direct coding of packs is the technology of choice.

The DMC of all labelled packs was scanned in order to check which serial numbers were used and to populate the central database. This registration process was carried out using serial number management software provided by Melior Solutions Limited.

Pack labelling and registration were conducted within the distributors' repackaging facilities in accordance with Quality Assurance Agreements in place between the respective manufacturers and distributors.

3.2.2 Distribution of coded packs

The supply of coded products to the participating pharmacies was provided by Tamro and KD Pharma. Both distributors kept coded packs in a separate stock so that these would not accidentally be shipped to pharmacies that did not participate in the project.

The regular ordering process between pharmacies and distributors needed to be somewhat changed for ordering of coded products. Products are normally ordered automatically by the pharmacies' stock management system on a daily basis once pharmacy stock drops below the ordering point. Discussions during the preparation of the pilot between logistics experts of the participating parties revealed that it was impractical to modify the automatic ordering system for the limited number of coded products and short period of the pilot. It was therefore agreed that the participating pharmacies ordered coded packs once a week by fax. The distributors delivered the ordered products on the following day.

3.3 Description of Information and Communication System

The EPVS is a system designed to enable users (pharmacies, doctors, wholesalers etc) to scan product packs and be provided with current product status or update current product status e.g. dispensed. Users of the system are only able to conduct product enquiries or, in the case of dispensing a product, update the current status of a specific product. Each enquiry or status update is an individual message/request. The system does not, for system security reasons, support batched enquiries.

Each user has a scanning point where each product pack making up a patients prescription is scanned to verify the product status. On scanning the pack code, the system interprets the data in the code and sends an enquiry message to the host system. The host system and associated communication systems have been designed to ensure that the response comes back to the user within one second of the product code scan taking place.

All requirements for the proposed system were collected and comprehensively described in the EFPIA User Requirements Specification (URS) [3] by an EFPIA expert team during the preparation of the pilot.

For the pilot the scanning points were all within pharmacies in and around the Stockholm area in Sweden, the data centre was in Germany.

3.3.1 Functionality

The system deployed was defined using numerous use cases. These are all described and defined in detail within the system Functional Requirements Specification (FRS) [4] and the system Technical Requirements Specification (TRS) [5].

Briefly these use cases covered the following functionality:

Manufacturer Scenarios:

- Data Upload
- Client Update
- Product Recall
- Reporting

Pharmacy Scenarios:

- Session Start-up
- Product Verification
- Product Dispense
- Product Receipt (special case for the demonstration system)
- Product Receipt Undo (special case for the demonstration system)
- Product Re-introduction
- Product Dispense Undo
- Product Removal

There were also numerous, technically detailed features of the system design that would allow it to be more easily deployed and adapted to different pharmacy system and workflow scenarios. In particular the system carefully delineated the host database and communication system from the pharmacy integration. By providing a 'communications gateway' component, that would be installed at each pharmacy, the overhead associated with logging, authentication, message parsing/formatting, online/offline capability (to account for loss of connection) and synchronisation etc. was removed from the pharmacy system design allowing each and every adaptation of the system to use a standard, fully tested host database connection mechanism. This was demonstrated by the use of the same communications gateway component in both the Swedish pharmacy integration scenario and the standalone laptop based demonstration interfaces.

3.3.2 System Architecture

During the pilot the EPVS was fully operated using one of two primary user interfaces, either the integrated Swedish ATS system or a functionally richer standalone system used by EFPIA personnel.

The architecture implemented utilised a communications gateway component which allowed significant amount of overall system functionality to be standardised in a single component and thus ease the integration of each interface adopted. Moving ahead, when other interfaces need to be adopted, this structure should provide a means to integrate with lower complexity and subsequent lower cost.

3.3.2.1 User Interfaces

The system design is such that each user group can have a different interface according to the need. Thus during the pilot there were two primary interfaces available:

- The fully integrated Swedish ATS Pharmacy system
- The portable 'standalone' demonstration system used by EFPIA personnel.

Critically however, the only difference between the two was at the interface level, all of the communications to the host were standard and identical using a gateway component to provide the layer between the host database and the user interface.

Pharmacist Interface

The interface provided for the pharmacists in Sweden was an extension to the existing ATS system used across Sweden by Apoteket. The integration team modified the ATS system to incorporate the ability to:

- Scan and interpret the EFPIA code during prescription 'picking' control.
- Perform pack verification at each scan during prescription 'picking' control and advise the pharmacist of the pack status.
- Caution the pharmacist if any pack returned a status other than 'available' when the prescription had been picked.

- Perform a 'dispense' operation on all products within EFPIA Pilot scope when the whole prescription is paid for or released from the pharmacy.
- Permit ad-hoc verification of product items without need of a prescription (for stock checking purposes)

The EFPIA enhancements were so tightly integrated with the Swedish ATS system that the workflow for the pharmacist was hardly altered, with the only extra requirements being:

- To check the status of the pack as the prescription was 'picked' and
- To ensure that all individual packs were scanned (occasionally, multiples of the same product might be scanned by means of multiple scans to the same physical product. This was actively prevented during the pilot).

To facilitate the use of the Data Matrix code used on each pack, new camera based scanning equipment was provided to the participating pharmacies configured to ensure that it was able to scan regular product via the linear code and EFPIA pilot product via the Data Matrix code. The new style camera based scanners were universally accepted as a vast improvement over the existing linear code only units.

The existing Swedish system architecture provided a means to permit all user consoles within a pharmacy to be routed through a single pharmacy based server. The server was enhanced with the new gateway component permitting communication with the EFPIA host system. The physical connection to the EFPIA host system was via a single VPN link dedicated to a single communications hub within the Apoteket IT infrastructure. All EFPIA pharmacy gateway components connected to the EFPIA host via the communications hub and along the single VPN link.

3.3.3 System Security and Protection of Data

In order that we could further assure the security of the system/data and provide known protection against threats, the team employed the services of an external agency known to one of the participating manufacturers.

The testing included internal and external threat analysis as well as internal and external threat testing, including a penetration test on the final system implementation.

The results of their processes and investigations are detailed within a separate document [6] which contains a complete summary of the tests carried out, the methodology employed and the results achieved. Some aspects of this document are of a sensitive nature and thus access to this document will be restricted.

The basis of the approach adopted by the external agency was:

- Identification of potential threats to those assets caused by the malicious intent of interested parties

- Identification of potential vulnerabilities derived from the system architecture
- Identification of vulnerabilities by scan and penetration tests of systems that may serve as entry points for an attacker (either internal or external to the system)
- Evaluation of any discovered threats and vulnerabilities by taking into account the:
    - Motivation of an attacker
    - The required knowledge, resources and preliminary access to perform the attack
    - The potential impact to the assets (exposure factor)

The output of the assessment was a register of risks per asset, which were marked as low, medium or high depending on the characteristics of the aforementioned criteria. The EFPIA senior expert team responsible for IT together with the system providers then assessed each notified risk and then applied the required corrective action or acceptance of the risk observed.

3.3.4 Quality Assurance

The project was carried out under Quality Management (QM) principles similar to GMP requirements. While it was decided not to go through a full formal qualification process for IT systems, project execution was conducted along the same principles including all phases of the V-model.

3.4 Operational Phase

3.4.1 Key figures

Key figures characterising the scope of the pilot are listed in Table 1:

Number of participating pharmacies	25
Total number of dispensing points in participating pharmacies	180
Number of dispensing points per pharmacy	2 to 10
Number of pharmacists participating in pilot	230
Number of manufacturers providing pilot products	14
Number of coded pilot products (Stock keeping units, SKUs)	25
Total number of coded packs	112.416
Number of coded packs per product	150 to 21.600
Duration of operational phase	4 months
Number of "verify" transactions	102.352
Number of "dispense" transactions[2]	95.523
Number of dispensed packs	95.049
Max. number of "verify" transactions in one pharmacy during	136
Max. number of "dispense" transactions in one pharmacy	126

Table 1 - Key figures on scope of pilot project[2]

Clearly, not all packs that were coded with the DMC before the beginning of the operational phase were marked as dispensed at the date when the operational phase was officially closed. The main reason for this is the different rate at which the products were sold during the pilot. Although the number of packs per article to be coded was decided based on a sales forecast for the participating pharmacies it was not unexpected that the actual sales number would be different from the forecast.

Another reason for packs not being marked as dispensed was the fact that some packs were sold without their DMC being scanned during picking control. Consequently, the pack could not be identified as being sold. As it could not be expected that the pharmacists would always remember which products carried a DMC they were reminded by ATS to scan the DMC after they had scanned the linear bar code instead of the DMC. Based on observations from the pharmacy log files it is apparent that in some cases there was still no DMC scan. The number of such cases is not known, it is estimated to be less than 5 % of all packs coded. It should be noted, however, that this effect is solely due to the pilot nature and the fact that all DMC coded packs did still

[2] The difference between the number of dispense transactions and the total number of dispensed packs is caused by two effects: (1) EFPIA used demonstration packs that were "dispensed" through the standalone demonstration systems. The number of dispense transactions includes the dispense of demo packs, but the total number of dispensed packs does not. (2) There were a certain number of packs that were dispensed more than once, cf. section 3.4.1.2.

carry the linear bar code. In a real world scenario it should be avoided that a pack carries two different codes because there would always be the chance that the wrong one is scanned.

3.4.1.1 System performance

To assess the performance of the Information and Communication System (ICT) the following criteria were defined:

System availability denotes the time the system is available to process any transaction in online mode, i.e. to provide an instant response to any verification or other type of user request. It is measured as the percentage of online processed transactions in relation to the total number of transaction requests. This definition is obviously a measure for the availability of the overall system while the availability of individual system components may still be higher.

The observed values of system availability for the complete period of pilot operation were the following:

Average of overall availability (for a total of 190.875 transactions)	99.8 %
Range of system availability for individual pharmacies	96.9 % to 100 %

System reliability denotes the ICT system's capability to provide the correct answer to any transaction request. It is measured as the percentage of transactions completed as expected in relation to the number of all transactions processed. It should be noted that this measure is related to the technical system only. It does not reflect any evaluation of errors or "exceptions" caused by incorrect use of the system. A list of this type of exceptions and a description of their specific causes is given in section 3.4.1.2.

It is clearly not possible to check for the correctness of each individual system response during the duration of the pilot. Therefore, the evaluation of system reliability was based on two informal and one formal analysis:

1. Feedback from pharmacists regarding erroneous system response
2. Random checks of recorded system responses
3. Checking system response when scanning codes of selected packs in three categories of 'unknown product', 'expired product' and 'recalled product'.

System response time is defined as the time that is elapsed between a transaction request, i.e. the scan of a DMC, and the instance when the system response is displayed on the user's screen. Table 2 shows percentages of measured response times split into four categories, i.e. less than 0.5 sec, between 0.5 and 1.0 sec, between 1.0 and 2.0 sec and higher than 2.0 sec. The overall average for all participating pharmacies over the complete duration of the pilot is given in the first row. Values for

the pharmacies with the shortest and longest response times, respectively, are shown in the following rows. It is obvious that even for the pharmacy with the slowest response time more than 99% of the transactions were completed in less than one second.

Pharmacy	RT < 0.5 sec	0.5 sec < RT< 1.0 sec	1.0 sec < RT< 2.0 sec	RT > 2.0 sec
Overall	94,4%	5,4%	0,2%	0,1%
Shortest	97,2%	2,6%	0,1%	0,1%
Longest	87,0%	12,2%	0,7%	0,1%

Table 2 - System response time for different pharmacies

3.4.1.2 Exceptions

A crucial component of a product verification system is exception reporting. Exceptions are defined as the occurrence of unexpected events. Unexpected events for the pilot project were defined as

1. **Verification, unknown pack:** Verification of a pack with unknown serial number and / or invalid expiry date and lot number
2. **Verification, previously dispensed:** Verification of packs with pack information (article number, lot number, expiry date, serial number) recorded to be already dispensed
3. **Dispense, previously dispensed:** Dispense of packs with pack information recorded to be already dispensed
4. **Undo dispense, conditions violated:** Undo dispense of packs for which the conditions to execute this operation are not satisfied (e.g. maximum allowed time elapsed after dispense)
5. **Undo dispense, not yet dispensed:** Undo dispense of packs that had not been dispensed before

Any of these events might be an indication for the appearance of a counterfeit product in a real world application. However, all of these events may also be due to incorrect use of the system. In any case, these exceptional events must be tracked. Also, an alert needs to be flagged to initiate a root – cause analysis of the more severe exceptions. An example for such a severe exception is definitely the occurrence of a dispense transaction on a pack that had been dispensed before.

Table 3 shows the number of occurrences of the exceptions listed above for all pharmacies over the complete period of operation.

Type of exception	**No of**

Verification, unknown pack	250
Verification, pack previously dispensed	373
Dispense, pack previously dispensed	283
Undo dispense, conditions violated	0
Undo dispense, pack not yet dispensed	4

Table 3 - Exception Types and Frequency

Understanding the potential causes of these exceptions will allow us to plan and design appropriate mechanisms to differentiate between real and false alerts.

A root-cause analysis of the exceptions that have been encountered during the pilot is available in the full report.

The discussion of the different types of exceptions shows that it is crucial for the credibility of a product verification system to correctly identify the causes for exceptions. Clearly, all exceptions must be identified and recorded to make sure that the occurrence of counterfeit products is captured. On the other hand, if there are too many alerted exceptions that are not caused by counterfeit packs but by some incorrect usage of the system, the system itself might be discredited. The generation of a large number of false alarms would render it impossible to differentiate between real and false alarms.

In order to avoid such a situation the system itself must be designed such that the workflow in the pharmacies is well covered. It is also recommended to categorise the exceptions. While all exceptions should be recorded in appropriate logs, only the more critical ones should be alerted. Eventually, there may be a need to develop algorithms for automatic identification of the most critical events.

It should be noted that the number of exceptions during the pilot can not be extrapolated to a full system as a substantial fraction of those was due to the specific pilot situation, e.g. the fact that the packs coded with the DMC carried the traditional linear bar code as well or the fact that it was agreed before the project that even in case of an alert the pharmacist was allowed to sell the pack.

3.4.1.3 Enhanced System Capabilities

During the pilot the team decided that to avoid issues concerning system validation it would not be appropriate to undertake real product recall testing, expired product detection or to inject 'known fake product' into the supply chain. To do so would have required the pharmacists to make product decisions based on the results displayed by the pilot system, which in turn would have required the system to be fully validated. Instead the approach adopted was to undertake a series of tests to demonstrate the system capability to detect products that were 'unsuitable for dispensing' at the end of the pilot as the system was being decommissioned from the pharmacies. In this way we

could still verify that the system performed as designed but would remove the need for the pharmacists to action the responses received.

To complete this process we introduced into the product supply packs that fell into one of three categories:

- Product that had expired
- Product that was placed under recall
- Product that did not exist on the system (a likely scenario for a fake)

As described, for logistics and regulatory reasons these packs were not introduced until after the Swedish phase of the pilot had concluded. This way we could better control the location and use of the packs created.

A total of 250 packs were created for each category. The pack codes for the expired and recalled products were uploaded to the EFPIA host system and once uploaded, the packs that were subject to a recall were indicated as such to the host. This is a simple process of changing the status of the product batch (or individual pack if required) by an authorised manufacturing client user. The simplicity associated with placing a series of packs/complete batch on recall should not be confused with a system that is not secure in this regard. Only the authorised owner of the packs is able to instigate this process, the comment regarding simplicity simply contrasts the EFPIA system mechanism with the present day mechanism for product recall. Given that affected packs are immediately placed into a recall state using the EFPIA system, it should be clear that the potential percentage recovery of affected packs should be high, tending towards 100% of packs not dispensed at that point. The packs with codes unknown to the system were simply printed and no accompanying data uploaded.

The test involved the simple task of using the system (client and host) in a live environment but instead of selecting and scanning real product, we scanned instead the controlled packs. The requirement was to ensure that the system correctly detected the presence of a pack with 'issues', correctly reported the issue to the operator scanning the product and subsequently a check was conducted to ensure that the relevant alert message had been generated by the system and sent to the appropriate recipient. During the test we ensured that products not falling into the affected categories were verified correctly to ensure that the system was reporting the correct response for the product scanned.

As expected, the system performed flawlessly and correctly indicated the presence of each of 250 products under recall, 250 products that had expired and 250 products that were 'unknown' to the system and thus could represent a counterfeit. The output from the client system, and sample email alert message are shown below.

4 User feedback

Equally important as the quantitative results presented in the previous section is the feedback obtained from the users of the EPVS.

EFPIA collected feedback from the participating pharmacists using two methods.

1. A web-based survey was sent to 230 pharmacists with a set of questions related to their general experience with the system. 123 responses were submitted.

2. In order to be able to discuss the results of the survey in some more detail a meeting was held with 5 pharmacists from different pharmacies. The feedback obtained through the survey was reviewed and a number of aspects were discussed.

4.1 Summary of survey results

The feedback provided by the pharmacists participating in the survey clearly shows that a large majority (more than 90%) of the responding users found the system easy or very easy to use. About 85% found the system response time "generally fast" or "consistently fast". Given the measured response times presented in section 3.4.1.1 (more than 99% of transactions completed within one second) it is a bit surprising that about 15% of respondents found the system to be "sometimes slow" or "too slow". This may be an indication that not only the technical response time was assessed but also other factors, i.e. workflow related aspects.

About three quarters of the respondents felt that using the EPVS system required no or only negligible additional effort in their daily work. Most of the remaining quarter found that there was some additional effort, but still acceptable. This is a very positive result and certainly reflects the fact that Swedish pharmacists are used to scanning each individual pack during picking control and that the EPVS functionality was fully integrated into the standard POS system.

Most of the reasons given by the pharmacists who felt that there was "too much additional effort" involved with the pilot are due to the specific nature of the pilot project: issues with supply of coded packs and with the fact that there was more than one code on the pack which caused some confusion. These issues were mentioned more frequently in response to the subsequent questions.

About 60% of the pharmacists had no problems at all when using the system. It is again the presence of two different types of code on the pack, which is the main source of trouble for the user. The main reasons why the linear barcode was scanned instead of the DMC were

- The fact that linear code and DMC were located on some products too close together and therefore the scanner picked up the linear code instead of the 2D code,
- That the pharmacist just overlooked that a pack carried the DMC.

If the linear code was scanned from a pack that also carried the DMC the system reminded the pharmacist to also scan the DMC. This meant some rework for the pharmacist. Unfortunately, there was a slight issue with the user interface in this situation, which caused additional trouble for the less experienced user and thus some more effort. The third category "scanning problem" includes rather unspecific answers that may also be related to the previously mentioned issue or scanning the linear code. The fourth category "scanning pack already marked as dispensed" is related to the "Dispense, previously dispensed" issue explained in section 3.4.1.2 and clearly caused confusion when it occurred.

All remaining issues are of minor importance and were perceived to occur very rarely.

The majority of the pharmacists understood the benefits of the approach although about 10% of the respondents explicitly stated that they do not see any benefits. Among the actual benefits mentioned were improved patient safety and security of the system. A very practical benefit in the daily work was the use of state-of-the-art scanners that were perceived to be more sensitive than the previously used ones.

The most important disadvantage was the fact that there was more than one code on the pack, which did cause some confusion in daily practice. This point was mentioned by about 20% of the pharmacists. The other main disadvantage was related to the specific supply process for coded packs that involved more work than normally necessary and led occasionally to a stock out situation for some of the coded products. This is clearly related to the pilot nature of the project and will not be relevant in a real world scenario.

It is worth noting that among the most frequently mentioned comments to this question was the statement that there is no disadvantage when using this system (15% of participants).

When pharmacists were asked for suggestions for improvement on the system, about a quarter of all responses provided were related to different minor aspects of the POS system's user interface. Also, quite a few suggestions were related to the aspect of different codes on the same pack. Some pharmacists explicitly asked to not use more than one code on a pack.

4.2 Feedback from pharmacy managers

In order to be able to discuss the results of the survey in some more detail a meeting was held with 5 pharmacists from different pharmacies. The feedback obtained through the survey was reviewed and a number of aspects were discussed.

The pharmacists present at the meeting confirmed the general feedback that the system was easy to use and did not require significant additional effort during daily practice. They also confirmed the superior performance of the new scanners.

It was clear to the participants that some of the problems mentioned during the survey, e.g. issues with product supply, were solely due to the pilot nature of the project. Some aspects were discussed in more detail:

- The pharmacists emphasised the value of getting more information in machine-readable form through the use of a DMC. They find it particularly helpful to get an automatic check of the expiry date and see this as a way to further increase patient safety by avoiding the dispense of expired product.
- Ideally, the pharmacists would like to receive more up to date information related to the physical nature of the product they are about to dispense, especially for products that are packed in tamper evident packaging. Examples are shape or colour of a tablet, which is of some relevance for certain patient groups[3].
- The EFPIA team had observed that in some cases (less than one percent of all verifications) pharmacists had entered the serial number manually into the system. The participants were not aware of the need to do this as they had not experienced significant issues when scanning a pack.
- The "double dispense" issue (see section 3.4.1.2) was discussed in detail. The reason for this occurrence was a slight deviation from the 'normal' dispense process that was not covered by the IT system. The occurrence of this issue was surprising and confusing for those pharmacists who were about to dispense a product and received the message that this pack was recorded as previously dispensed. Clearly, such an issue must be eliminated in a real world system as its occurrence may discredit the whole system.
- Inspired by the "double dispense" issue it was discussed that clear procedures must be defined in a real world application for situations in which a valid warning is issued by the system.

[3] This type of information can obviously not be provided by an optical code, but would require an online query in a database.

5 Key Project Results and Conclusions

The technical results from the pilot project were presented in section 3.4.1 and the feedback collected from the users in section 4. The purpose of this chapter is to summarize all results and experiences, draw conclusions and discuss these.

5.1 Key Results

Following is a list of the key results identified from the experiences gathered during the EFPIA pilot project:

KR1 The model EFPIA supports for "Product Verification at the Point of Dispense" works in practice.

KR2 It allows for effective identification of fake packs as well as expired packs and recalled products.

KR3 The observed system availability and performance allow pharmacists to work at normal pace and without significant additional effort.

KR4 The system is easy to use when fully integrated into the pharmacy workflow and existing pharmacy Point of Sales system.

KR5 The two previous aspects lead to very high user acceptance.

KR6 In order to achieve sustained credibility, the system must provide the correct answer to all transaction requests.

KR7 The system should be customised to the existing pharmacy workflow as well as local conditions and regulatory requirements. It is recommended to run a pilot phase for each deployment (region) so that defects can be eliminated before full roll-out.

KR8 The presence of more than one code on the pack causes confusion for the user and will jeopardise user acceptance.

KR9 The necessary data segregation and data security can be technically ensured.

KR10 Pharmacists are highly interested to get expiry date and batch number in machine readable form.

5.2 Discussion and assessment of the Product Verification Approach

Using the pilot results and key learnings listed above now allows to assess the concept tested in the pilot:

Effectiveness: The system is able to identify falsified, recalled, and expired packs. This can be expected as well from systems that are based on different system structure, like Track&Trace systems, or are using other data carriers.

Reliability: Overall system reliability hinges on flawless execution of required work flows, the quality of the IT system and the sustained readability of the data carrier used. The pilot has shown that the work processes in a pharmacy can be very well accommodated.

User acceptance: In the product verification the only relevant user groups are retail and hospital pharmacists as they are required to verify the status of products that are about to be dispensed. The pilot project has shown that a very high level of user acceptance can be reached.

Data security: The proposed system involves the least required number of participants compared to most other approaches. Only registered stakeholders need to get access to the system so that access to the system can be controlled more effectively compared to a system in which patients might be involved. This allows for the highest achievable level of data security if state-of-the-art security technologies are employed.

Identification of a source for illicit or substandard product: While the EFPIA system is definitely capable of identifying an illicit or substandard product before it is dispensed to the patient, it cannot be used for automatic identification of the entry point of a suspect product into the legitimate supply chain. Instead, an investigation has to be initiated should an alert be flagged by the system to check for the underlying reason and to search for patterns that may help to identify the source of the problem. A full Track&Trace system will help to identify such a source much quicker as it covers not only the end point of the supply chain, but also intermediate points. Clearly, this is only true if a very high standard in data quality of the Track&Trace system can be maintained.

5.3 Experiences and Discussion

The purpose of this section is to review some general experiences gathered during the preparation and execution of the project. This seems appropriate as the results of such a project clearly depend on the "political" and technical environment in which it is carried out.

5.3.1 The political environment

From the beginning, the concept proposed by EFPIA was based on the idea of cooperation between the different stakeholders in the pharmaceutical supply chain. Ensuring patient safety by a traceability system that involves the participation of several stakeholders must not only be based on a set of rules but also the willingness and ability to cooperate.

Given the respective interests and concerns of the different stakeholders who are required to participate in a full product verification system it is apparent that a well-defined legislative framework is required to enable a system that is acceptable for all parties. An alternative to this approach might be one based on voluntary participation. It must be expected, however, that such a system will not be used to the full extent and will leave open backdoors for those who want to introduce illicit products to the market.

5.3.2 The technical environment

There are two main aspects regarding the technical environment of the project that should be discussed.

The first aspect is the technical situation of pharmacies in Sweden. The healthcare system in Sweden is supported to a large extent by IT systems. An example is the high portion of e-prescriptions (approximately 80 %) in the Swedish market. Also many other processes in and around the pharmacies are strongly supported by IT systems. The PoS system of Apoteket called ATS, is installed in all pharmacies and the same version is used everywhere. This system has online links to remote systems, e.g. for real-time reimbursement management and automatic ordering of products from distributors.

It was advantageous for the execution of the pilot to find such a well developed and standardised environment. But it was equally important to find established workflows that involve regular scanning of barcodes during the dispense process. This enabled seamless integration of the EFPIA front end application into the work flow as well as into the IT system. Also, this situation allowed for a very short period required to implement the solution.

One obvious prerequisite for such a system is the availability of a broadband data network connection into each pharmacy. It is obviously desirable to integrate the front-end part of the verification system into the existing point of sales application. On the other hand, this is not absolutely necessary as the solution employed for the EFPIA pilot can be used very well in its standalone version without any additional effort. The experience gathered from the operational phase shows that even in such a friendly environment there is still some room for small defects, especially the "double dispense" issue described in section 3.4.1.2. Such an issue can cause severe damage to the overall system in the long run as it can cause the user not to trust the system response and thus render the whole system useless.

When implementing a full system for regular use it is not sufficient to execute the project along well accepted quality management procedures as has been done for the EFPIA pilot. It is necessary to also run a pilot project limited in scope and time that can be carefully monitored to identify and eliminate any flaws before the system is fully rolled out to an entire market.

Appendix A: Abbreviations

Acronym	Full text
ATS	Apoteket Terminal System
CIP	Club Inter pharmaceutique
COTS	Commercial-off-the-Shelf
DMC	Data Matrix Code
EFPIA	European Federation of Pharmaceutical Industries and Associations
EPR	Electronic Patient Record
EPVS	EFPIA Product Verification System
FRS	Functional Requirements Specification
GTIN	Global Trade Item Number
IT	Information Technology
NTIN	National Trade Item Number
PoD	Point of Dispense
PoS	Point of Sale
PZN	Pharmazentralnummer
RFID	Radio Frequency Identification
TRS	Technical Requirements Specification
URS	User Requirements Specification
VPN	Virtual Private Network

Appendix B: Citations

1 European Pack Coding Guidelines, V 2.1

2 Randomisation Test Bed V 1.1

3 EFPIA Product Verification Project: User Requirements Specification - Hosted Data Exchange and Processing System, V 2.1

4 EFPIA EPVS Pilot Project Functional Specification, V 2.4

5 EFPIA EPVS Pilot Project Design Specification , V 1.5

6 EFPIA-Assessment-report-1.0.2.pdf