

ANNEX 2: Stocktaking Reports

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1 EXECUTIVE SUMMARY

Introduction

- 1.1 The attached briefing papers are those required from Europe Economics to complete its study for DG Enterprise and Industry of some of the likely impacts of policy options designed to combat the risk of counterfeit medicines and to ensure that unsafe medicines are not supplied through parallel trade (Specific Contract No S12 446433 under contract ENTR 04/093 LOT 4). The four papers follow more urgent work in April and May in preparing the main impact assessment, and only limited time was available under the contract for their research.
- 1.2 The objective of the four papers is to provide an initial stocktaking to help to guide DG Enterprise and Industry in planning its further work in this area and not to present detailed analysis and firm policy recommendations. DG Enterprise and Industry accepts that the resource available must be limited, and that it would not be proportionate to require an in-depth study such Europe Economics has previously made of other issues under this contract. The four reports are seen as “stock-taking” exercises, the conclusions of which would be the identification of gaps in what is known and issues for possible further work by DG Enterprise and Industry rather than to make firm policy recommendations.
- 1.3 The stocktaking by Europe Economics reviews the following four issues:
- Rapid Alert Systems
 - On-line Pharmacies
 - Clinical Trials
 - Track & Trace Technology
- 1.4 The features of the current situation that are most relevant to these issues are:¹
- The risk of counterfeit prescription medicines being supplied through the conventional supply chain to patients in the EU is increasing and should be taken more seriously than in the past.
 - There is a major risk of counterfeits being supplied to other parts of the world after transit through the EU; this is just one aspect of the fact that counterfeiting of medicines is a global problem.

¹ The situation is described and analysed in detail in other work by Europe Economics and by DG Enterprise and Industry.

- The division of legal responsibilities between EU institutions, national governments, and international organisations means that effective action requires collaboration and cooperation of policies and of policy implementation.
- The phenomenal growth of use of the internet has led to a high proportion of drugs sold online and delivered by post being potentially counterfeit. Many of these drugs are “recreational” or other products that can legally be sold over the counter without a prescription, but some are medicines normally supplied by pharmacists on prescription.
- The practice of parallel trade within the EU leads to conditions which facilitate illegal trades. Patients as whole suffer significantly a result of parallel trade; the support for the practice by the European Commission in the past probably rested on a view that any form of competition can be assumed to bring benefits; but this is not true in the case of prescription medicines. It follows that policies resulting in any reduction in parallel trade features in the analysis as a benefit and not as a cost to the welfare of EU consumers.

Overview

Rapid Alert Systems

- 1.5 The Council of Europe has suggested an adaptation of the form used for RAS between EU and some other regulatory authorities of defective medicines, and this adaptation is currently being considered by the EMEA and national competent authorities (CAs). A proposal has also more recently been made by the Danish Government for a more effective system or systems. These suggestions should be properly evaluated and a sound plan formulated and pursued as a matter of some priority.
- 1.6 There appear to be no immediate plans for a RAS that could be used by medical experts and by patients (as opposed to regulatory authorities) throughout the EU to notify their competent authorities about possible counterfeit medicines.² In this respect the EU lags behind the WHO Western Pacific Region.
- 1.7 There is no obvious justification for any increase in expenditure in IT by EMEA or others until policy makers have settled what should be the subject of RAS, and between whom the information should be transmitted.
- 1.8 It might be appropriate for an urgent study to be commissioned jointly by the Commission, the WHO, and the Council of Europe to give focus and emphasis to this issue and to make practical proposals.

² Some national authorities are instituting such a system, e.g. the MHRA in the UK.

Clinical Trials

- 1.9 An incident was detected in the UK in 2007 of counterfeit medicine infiltrating a clinical trial. Quite apart from harm to participants, the potential damage to patients were such incidents to occur without detection would be very large; wrong decisions from the trials might be made.
- 1.10 Policies in this area should seek the highest safety standards. The regulations governing clinical trials should be made more stringent, to ensure that nothing is used that is not authentic.

On-line Pharmacies

- 1.11 The ECJ ruling in 3003 in the DocMorris case has resulted in an unsatisfactory situation, in which the ruling would appear to take community law further into the area of healthcare provision than was intended by the Treaty, and in which practices between Member States may vary with regard to the sale of prescription medicines (which may or may not be allowed to be sold over the internet /by mail order) and other pharmacy medicines (which may not be prevented from being sold in this way even though that was regarded by many governments as unsafe or otherwise undesirable for their circumstances.)
- 1.12 Policy options for consideration include legislation to remedy this situation.
- 1.13 The ECJ ruling rests on a purely legal analysis, with little discussion of healthcare issues or of subsidiarity. Similar weaknesses appeared in ECJ rulings in other cases relating to trade in pharmaceuticals. This raises a large question of how the ECJ can be helped to consider more fully the social and economic (including healthcare) implications of the issues it has to address in the area in which trade policy and healthcare intersect.

Track & Trace Technology

- 1.14 In order to combat counterfeit prescription medicines, the most effective technique would be to allow the person supplying the patient – the qualified pharmacist or medical professional (doctor or nurse) – to check that the pack being dispensed is authentic. This is now possible through the use of IT systems that allow each individual pack to be uniquely numbered, and for the number to be checked as the pack is dispensed.
- 1.15 If the EU legislates in this area, or makes recommendations to Member States for action in areas within their competence, any legislation should probably require the delivery of objectives – the identification by the person immediately supplying the patient of the uniquely identified pack as having been manufactured in an approved batch by an authorised manufacturer – and not the technology to be used.
- 1.16 It is not necessary for the pack to have each step in the distribution chain recorded and identified (a product pedigree), although if this were done – as is also technically possible – then it would be easier to discover the weak link in the chain should any adverse events occur.

- 1.17 There is no track & trace technology that would protect the individual purchasing OTC drugs over the internet, or at clubs, bars, health spas and other unlicensed premises.

2 RAPID ALERT SYSTEMS

Object of report

- 2.1 This report is one of four required from Europe Economics to complete Specific Contract No S12 446433 under contract ENTR 04/093 LOT 4, for assessment of the impact of policy options to combat counterfeit medicines and to ensure safety of medicines delivered through parallel trade. The four briefs follow high priority work delivered in April and May 2008.
- 2.2 This report is to
- “provide a stocktaking of various rapid alert systems with respect to objectives and needs (e.g. Community RAS (Compilation of Community Procedures), food sector (RAPEX), Working Group of Enforcement Officers (WGEO), Council of Europe, WHO), and to assess the impact of a database on Rapid Alert Messages on Counterfeits and others.”
- 2.3 A detailed assessment is not required, but a brief overview of where the Commission's policy work might benefit from further understanding and analysis.

Context

- 2.4 DG Enterprise and Industry is developing policy proposals designed to reduce the risk of counterfeit medicines and unsafe medicines supplied through parallel trade. One way of reducing the risks would be to ensure that systems for the rapid alert of regulatory agencies, patients, medical staff and businesses involved in the supply chain to any defective / counterfeit products are working as efficiently as possible.
- 2.5 If more resource is to be put into this area, it would not have been as a result of the Heads of Medicines Agencies Strategy Paper, November 2007, which did not mention the issue (although it did “support the EU telematics strategy” and mentioned the desirability of developing “additional systems necessary to optimise the exchange of information and communication at all levels of the regulatory system within the Network”).

General Objectives of a Rapid Alert System

- 2.6 A Rapid Alert System (RAS) may be defined in terms of
- What kinds of information are to be conveyed.
 - By whom, to whom and with what purpose.
 - By what means.

Types of information

- 2.7 Information that is provided through a RAS might be of *suspected* counterfeit or otherwise defective prescription medicine; OTC medicines; or health foods (there may be a blurred line between health foods and medicines).
- 2.8 Alternatively, the information might be limited to *cases in which the product had been found to be counterfeit or defective following an investigation* by a competent authority (CA), and of steps taken in response to this. This is the sense in which the term is generally understood within the EU, as there is an existing RAS (discussed below) that is purely for communication between staff of regulatory authorities, and then – when it is clearly necessary – to alert the public and traders to the need for a product recall.

Who should be alerted, by whom and with what purpose?

- 2.9 Currently, most rapid alert systems in place involved communications between government regulatory agencies. However, recent trends have pointed to creating a second type of RAS – a broader system involving medical professionals, supply chain members, and the public in the RAS so as to increase the efficiency of the alert. This would be for consideration as part of policies concerned with public awareness.

What means of communication?

- 2.10 This might be anything from a standard form sent over the internet to a telephone call or letter, or public announcements.

Characteristics of RAS designed to combat counterfeit medicines and ensure any medicines supplied through parallel trade are safe

- 2.11 The starting point is that:
- The problem of counterfeit prescription medicines supplied through pharmacies and hospitals is not yet widespread but a high proportion of medicinal products sold over the internet and supplied through the post may well be counterfeits.
 - There is probably not yet as much awareness in the EU among medical professionals, regulators or the public of the danger of counterfeit medicines as there should be, since the problem appears to be growing significantly but from a low base.
 - Regulatory authorities in the EU have no effective means of tracing medicines through the supply chain, partly because of parallel trade and the 'grey market'.
 - The information leaflets provided to patients in packages of medicine do not include clear guidance about how to register a complaint or a concern with the authorities.
- 2.12 Against this background, the characteristics of an effective RAS for the purpose of transferring information between regulatory authorities are that it should be able to include

features particularly relevant to counterfeit investigations, as well as to products found to be defective for other reasons. The staff concerned with criminal investigations are often not the same as those dealing with product inspections; and the information may be needed at a different stage.

2.13 With regard to the broader problem of counterfeits supplied directly to the public, reducing the risk of harm to patients from either counterfeits or medicines that are unsafe for other reasons are:

- Its scope should be wide, covering all medicines, including those sold over the counter and over the internet as well as prescription medicines supplied through the legitimate supply chain. Borderline products (such as health foods) should be able to be included. It should cover products suspected to be defective as well as those for which there is proof.
- It should be available to the public and to medical professionals as well as to regulators (obviously with differences in the information conveyed, or perhaps in two forms – two separate systems).
- It should be international in scope.
- It should use a standard, easily read and completed form that can be transmitted over the internet, and also any other means of communication.

2.14 Some existing RAS are now summarised.

EU and other systems

Community RAS (Compilation of Community Procedures)

2.15 The EMEA is responsible for maintaining and publishing the Compilation of Community Procedures, which is a collection of GMP-related procedures and forms agreed by the GMP Inspectorates of all the Member States. Article 3 of the GMP Directive, 2003/94/EC requires Member States to take account of the procedures. The procedures include arrangements for RAS between competent regulatory authorities (CAs) but not between medical professionals or the public and the authorities.

2.16 Coverage of this RAS includes animal as well as human medicinal products, but excludes pharmacovigilance.

2.17 The CA in a country in which an apparent defect or other problem is identified has to assess its seriousness, and if it justifies a Class 1 or Class II recall, to notify all other CAs

in the EEA, plus members of CADREAC,³ PIC/S,⁴ EDQM and Mutual Recognition Agreement (MRA) partners (i.e. Australia, Canada, New Zealand and Switzerland). Standard forms are suggested, but there does not appear to be a standard facility for returning them on-line. The system appears well established but information provided is not specifically focused on counterfeits.

PIC/S

2.18 The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) published a guide to Rapid Alert Systems in September 2007 (reference P 1010-3: "Standard Operating Procedure: Procedures for handling rapid alerts and recalls arising from quality defects"). This is copied from the EU document with a similar title that was published in May 2000, and will be revised if and when the EU document is revised. It covers medicines for humans and animals but excludes information arising from pharmacovigilance.

2.19 The contact list of those to whom alerts should be sent is kept by the EMEA.

RAPEX

2.20 RAPEX is administered by DG Sanco. It is the EU rapid alert system for all dangerous consumer products, with the exception of food, pharmaceuticals and medical devices. It covers both measures ordered by the national authorities and measures taken voluntarily by producers and distributors.

2.21 The legal basis for RAPEX is in GPSD article 12.

2.22 The method of operation is that if a product is withdrawn from the market in any Member State the RAPEX contact point in that country immediately informs the RAPEX contact point in the Commission, who then disseminates the information to all other EU Member States.

2.23 There is an agreement with an authority in China under which any product safety issues found with Chinese products is communicated, so that the Chinese authority can investigate.

2.24 There does not appear to be any particular means of communication (no standard form or electronic link).

³ Collaborative Agreement between Drug Regulatory Authorities in EU Associated Countries. There is an organisation called new CADREAC that includes central and eastern European countries; not clear yet whether these countries are included in the RAS.

⁴ The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme are jointly referred to as PIC/S. This organisation seeks to encourage use of GMP standards. Members include Argentina, Australia, and others but not the USA. The WHO is a member or associated.

RASFF

- 2.25 The Rapid Alert System for Food and Feed (RASFF) has its legal basis in Regulation EC/178/2002. It is administered by DG Sanco.
- 2.26 Under this system, any member country (the EEA countries) that identifies a problem on which it needs to take action informs the EC, which in turn again evaluates and passes information on to member countries, to EFSA and EFTA, and to countries outside the EEA when appropriate. Problems may be identified either from market surveillance, from customs, or from the public, and are then reported to the national competent authority. However the RASFF is limited to regulatory authorities, like the other EU RAS reviewed here.
- 2.27 In the latest Annual Report, the Health Commissioner Markos Kyprianou, claimed that the RASFF was “one of the great success stories of the EU’s integrated approach to food safety”.

Heads of Medicines Agencies’ Working Group of Enforcement Officers (HMA WGEO).

- 2.28 The Heads of Medicines Agencies (HMA) is an informal group established by the Member States.⁵ The HMA WGEO is the group of heads of enforcement within the agencies (enforcement is a distinct function from inspection; the inspection staff would probably have responsibility for RAS of defective medicines, but not be responsible for counterfeit or other criminal investigations).
- 2.29 The Council of Europe recommendation for an addition to the Community RAS (see below) specifically designed to report suspected counterfeits was supported by the WGEO. It was then referred by the EMEA to a group representing inspection staff, who saw practical and legal difficulties, so that nothing has yet been decided. If it is not possible to integrate the systems, the HMA WGEO may try to set up a parallel system for counterfeit alerts.
- 2.30 Given HMA’s status, HMA cannot fund it nor adapt its computer systems to meet its requirements unless through complex agreements between Member States. EMEA and the Commission lack a legal basis for spending on enforcement of criminal law, which is one of the reasons why an initiative was needed from the Council of Europe.

RAS in pharmacovigilance

- 2.31 There are arrangements whose legislative base is Directive 2001/83, under which MS that discover from pharmacovigilance arrangements that there are previously unknown risks from the use of a medicine are able to inform other MS. There is a standard form, and process for doing this.

⁵ Contact person Mr. Hugo Bonar at Irish Medicines Board: tel +353 1 634 3431

2.32 These arrangements were last reviewed in 1996.

Council of Europe, EDQM

2.33 The European Directorate for the Quality of Medicines and Healthcare (EDQM) is a Directorate of the Council of Europe, in Strasbourg.

2.34 The Council of Europe, having perhaps a wider remit than the EC with regard to health and criminality, took the view that the RAS form used by the EMEA and PIC/S was not well suited to reporting counterfeits or other criminal activity, and so designed a new form “Counterfeit Medical Product Notification” (May 2005) as an adaptation of the EMEA form. This can be sent electronically.

2.35 The Council of Europe does not have its own list of addressees, but recommends the form be sent to the appropriate address list. It is intended for use by the same organisations that use the EMEA and PIC/S forms.

Summary table:

Characteristic	Does it meet suggested criteria?	Comments
Coverage	No	Same as Community RAS
Availability	No	“” “”
International scope	Undefined	
Ease of use	?	Better than EMEA/PIC/S but probably not very easy

(a) The Council has taken some other steps in this area. According to Mrs Sabine Walser of EDQM:

“...the EDQM’s Committee of Experts on minimising public health risks posed by counterfeiting of medicines and related crimes has been entrusted with a special work programme on the action to take to combat the counterfeiting of medicines and related crimes, by putting forward a set of coherent measures, comprising model approaches, multi-disciplinary co-operation between the sectors concerned, the setting up of a special information system in this field and the concept of regular training. This programme is based on and continues the activities of the former Ad hoc Group on Counterfeit Medicines (Partial Agreement in the Social and Public Health Field).”

2.36 Other steps taken under the auspices of the Council of Europe include:

(a) In 2005/06 the Council suggested a model for a network of dedicated contact persons (“single points of contact”, or SPOCs) within regulatory authorities involved in combating counterfeits and other forms of pharmaceutical crime. There would be SPOCs in the police, customs and government departments as well as a National SPOC in the medicine regulatory authorities. In 2007 the WHO adopted this model and recommended it on a global basis.

- (b) Over the last two years the General European Official Medicines Control Laboratories (OMCL) Network (GEON), which is coordinated by EDQM, has developed a rapid information exchange system with the aim to share information on test methods/analytical techniques used for the detection and testing of counterfeit medicinal products and illegal medicines. Information is stored on an IT platform (OMCLnet) with controlled access which for the time being is restricted to OMCLs.
- 2.37 This system is complementary to the Rapid Alert System (RAS) for information exchange of quality defects between the Competent Authorities of EU/EEA member states, CADREAC, PIC/S, EDQM and MRA partners. By June 2008 about 150 analytical reports from 18 OMCLs, which are prepared in a standardised format, have been made available via OMCLnet to the members of the Network.
- 2.38 In 2004 the 'Official Control Authority Batch Release Certificate' (OCABR) Network was established. If a batch of immunological medicinal product or a medicinal product derived from human blood or plasma is found not to comply with specifications, this information shall be provided, by a rapid information exchange mechanism, to specified contact persons within the European Community Network. Details of the non-compliance are made to other Member States upon request. The OCABR network today includes 31 Member States and Countries.

WHO Europe

- 2.39 The WHO Europe Region does not appear (from its website) to do anything in the field of RAS.
- 2.40 The WHO IMPACT study has not yet produced any recommendations in this area.
- 2.41 WHO may have a global RAS but it is apparently not well regarded or much used – for example, our understanding is that the EU and FDA do not file information there.

WHO Western Pacific Region

- 2.42 The WHO Western Pacific Region has a Rapid Alert System focused on combating counterfeits.
- 2.43 This RAS is a moderated electronic communications network involving the designated focal person and representatives of countries and areas in the region, WHO and partner organisations. The system transmits information on cases of counterfeit medicines in an effort to alert authorities, so that they can take timely action.
- 2.44 The system was instituted by the Western Pacific Region of the WHO in collaboration with partner organisations as part of implementation of the Regional Strategy for Improving Access to Essential Medicines in the Western Pacific Region, 2005 – 2010.
- 2.45 The objective is not only the rapid transmission of information but the encouragement of the relevant authorities to take action when needed.

- 2.46 It works through an electronic report form (in English), well designed and apparently easy to complete. Reports are reviewed by a moderator, who passes them on as appropriate.
- 2.47 The system was set up in recognition of the international nature of counterfeiting; the reason it was limited to the Western Pacific was presumably institutional. It may be extended in time to other regions.
- 2.48 Note that the system is focused just on counterfeit medicines, not batch recalls for other reasons (though the system would presumably be used if there were other serious episodes requiring product recalls).

Summary table:

Characteristic	Does it meet suggested criteria?	Comments
Coverage	Yes	
Availability	Yes	
International scope	No	Limited to the WHO Region
Ease of use	Yes	

Danish Medicines Agency

- 2.49 The Danish Medicines Agency has proposed establishing a Rapid Alert System for Counterfeit and Illegal Medicinal Products in the Illegal Distribution Chain, as a supplement to the system for Rapid Alerts and Recalls Arising from Quality Defects and the Rapid Alerts and Non-Urgent Information System in Pharmacovigilance.
- 2.50 Rapid alerts in this third system would cover counterfeit and illegal medicinal products in the illegal distribution chain as well as other relevant alerts. The information in the system would be co-ordinated with all other systems to ensure that all information would be available to all Competent Authorities in the Network and that relevant information is reported to other systems.
- 2.51 Currently the Danish Medicines Agency employs at least eight different systems. Of these, only the Rapid Alerts and Recalls Arising from Quality Defects and the Rapid Alerts and Non-Urgent Information System in Pharmacovigilance are well-defined and well-functioning systems. The other systems are not well-defined resulting in lost time and resources and in duplication of alerts.
- 2.52 Alerts in this new third system would be sent from one Competent Authority to all Competent Authorities in the Network and all Competent Authorities in the Network should report through this system.
- 2.53 The co-ordination function would save resources among Competent Authorities and avoid duplication of information across all systems in the network.

- 2.54 In order for the third system to be efficient it would need to be developed in close co-operation with sectors responsible for enforcement, customs, and pharmaceutical supervision.

Conclusions: policy initiatives for consideration

- 2.55 Except to the extent that the CoCP system is relevant to counterfeits it appears that the issue of RAS as a means to combat counterfeits has so far been given only low priority by any of the international organisations reviewed here (more is being done by some national regulatory agencies). The current Community RAS is not specifically designed for combating counterfeit pharmaceuticals. International organisations may consider defining separate RASs for separate cases (i.e. Counterfeits, Defects) and expanding the scale to include stakeholders beyond regulatory agencies.
- 2.56 WHO IMPACT has produced little in this area; the EMEA has been considering for some time a minor adaptation of its forms suggested by the Council of Europe but it seems that nothing is in the pipeline that would make any significant difference – this would only come if:
- (a) a form was made available to medical professionals and to the public who suspect that they have been supplied with counterfeits through any channel, including over the internet or through the post;
 - (b) if communication between regulatory authorities at various levels (inspection, enforcement, customs) about established cases of dangerous and/or counterfeit medicines were organised on a global basis, presumably through the WHO; and
 - (c) the RAS between regulatory authorities is able to encompass suspected incidents of counterfeiting.
- 2.57 Any form available to the public would have to be for submission to a national regulatory authority for evaluation (this system has been introduced in the UK in a low-key way and is being considered in Ireland, and perhaps elsewhere) but the EU or Council of Europe could act as facilitators and offer a model or technical advice to any country interested, either as MS or through the WHO.
- 2.58 The Commission could also probably do more to speed up the introduction of a system of RAS within the EU for cases where counterfeits had been found, perhaps building on the proposals from the Danish Government.
- 2.59 There is no reason to think that more IT spending would be justified in the EU until the authorities have defined what it is that should be communicated

3 ONLINE PHARMACIES

Internet Trade in pharmaceuticals

Introduction

- 3.1 Four brief reports are required from Europe Economics to complete Specific Contract No S12 446433 under contract ENTR 04/093 LOT 4, following the high priority intensive work in April and May 2008.
- 3.2 The present report is to consider the issue of possible harmonised provisions in pharmaceutical legislation for internet trade with pharmaceuticals.⁶ A short 'stock-taking' is required to help to suggest future directions for policy work rather than detailed analysis leading to firm conclusions.
- 3.3 The relevant documents include the judgment in the DocMorris case (case C-322/01, see below) and information about practice in different Member States.
- 3.4 Many counterfeit medicines are sold in the EU over the internet, in small packages, without much likelihood of detection. The use of the internet increases the difficulties for the authorities of tracking down and inspecting suppliers. This reinforces the traditional reasons for regulation of those supplying medicines.
- 3.5 Although there is a lack of evidence to date, it may be assumed that criminals introducing counterfeits into the supply chain for prescription medicines could use apparently legitimate businesses to cover their activities; for example by holding licences as pharmacists, wholesalers, parallel traders or other legitimate organisations, any of whom may purchase or sell medicines over the internet.
- 3.6 Supplying medicines by internet and mail order may carry high risks to patient safety. The absence of face to face discussion with a doctor or qualified pharmacist must increase the risk of patients misunderstanding (or not receiving) guidance on the safe use of medicines. The legal systems of many countries have therefore traditionally limited sales of medicinal products (including some non-prescription medicines as well as prescription medicines) to supplies through licensed pharmacies or hospitals.
- 3.7 Furthermore, these risks are compounded by a lack of consumer awareness regarding the risks of online pharmacies. Research conducted by the Royal Pharmaceutical Society of Great Britain (RPSGB) showed that nearly a third of consumers have no knowledge about regulations governing online pharmacies.

⁶ Others relate to Rapid Alert Systems, clinical trials, and track & trace technologies.

- 3.8 Medicines can generally be divided into three classes that govern their sales. In the UK, for example, the Medicines Act of 1968 defines the categories thus:
- “Prescription-only medicines” – can only be sold or supplied by a pharmacist if supplied by a doctor.
 - “Pharmacy medicines” - can be sold without a prescription but only by a pharmacist.
 - “General Sales List medicines” - can be sold by any shop, not just a pharmacy.
- 3.9 The E-commerce Directive (2000/31 of 8 June 2000) allows derogations from the basic principle that e-commerce must be allowed where such derogations are necessary for the protection of public health.
- 3.10 The Distance Selling Directive (97/7 of 20 May 1997) allows Member States to introduce or maintain more stringent provisions to ensure a higher level of consumer protection. Article 14 states that
- “such provisions shall, where appropriate, include a ban, in the general interest, on the marketing of certain goods and services, particularly medicinal products, within their territory by means of distance contracts, with due regard for the Treaty.”

Risks associated with mail order sales of medicines

MarkMonitor survey (2007)

- 3.11 Detail of the risks associated with the mail order sales of medicines was provided in a study by an internet consultancy, MarkMonitor, published in August 2007. Annual sales of online pharmaceuticals were estimated at \$4 billion. The study concluded that rapid growth in unlicensed online pharmacies is putting the health and safety of millions of consumers worldwide at risk.
- 3.12 Markmonitor investigated 3,160 internet-based pharmacies, and traced back the servers to host countries; 16 per cent were British-run, second only in number to no less than 59 per cent coming out of the United States.⁷⁸ MarkMonitor also found that nearly two-fifths of spam e-mails offering popular medicines — and nearly one third of online suppliers to wholesalers --- were Chinese.
- 3.13 A “tiny fraction” of the online British pharmacies were certified by the RPSGB, Great Britain’s pharmaceutical regulatory authority.

⁷ The Times (2007): “Online drugs put patients at risk” <http://www.timesonline.co.uk/td/news/uk/article2288778.html>

⁸ The Financial Times (2007): “China dispenses two-fifths of drug spam” <http://www.ft.com/cms/s/0/f3d98d12-4f7e-11dc-b485-0000779fd2ac.html>

- 3.14 The most popular drugs examined in the study were on sale for one fifth of the price at which they are sold by registered pharmacies.
- 3.15 Such cheap availability immediately stirs suspicions of counterfeit pharmaceuticals. According to the Chief Executive of MarkMonitor:
- “Our findings indicated that some of the drugs being sold on these sites may be fake, expired, diluted or alternatives”.
- 3.16 Moreover, 50 per cent of all pharmacies surveyed had inadequate customer protection information such as PILs or expiry dates. Even for a self-prescribing consumer, this is likely to lead to confusion and anxiety, if not worse.
- 3.17 The MHRA has introduced new measures to register and identify websites that sell approved or legal medicines. This uses an authorised logo that is linked to the register of firms. However it would presumably not be difficult for a counterfeiter to imitate such logos.

Legal position in different European countries

Review by German Government, Dec 2007

- 3.18 Dr Niels-J Seeberg-Elferfeldt of the Federal Ministry of Health in Germany wrote a report ‘Mail order trade in medicines from the EU, EEA and Switzerland’ (December 2007). The purpose of the report was to advise the German Government whether the safety standards required in other countries were equivalent to those in Germany.
- 3.19 The motivation for the report is set out as follows (with emphases added):

According to the official reasoning for Section 73 (1) sentence 3 *AMG*, the publication of this overview seeks to provide guidance to consumers who wish to purchase medicinal products from EU and EEA countries and thus serves to protect German consumers. It can only provide information on which of the listed states have safety standards comparable to those ensured under German law at the time they are overviewed by the *BMG*. In a ruling of 20 December 2007 (file number: I ZR 205/04) **the Federal Supreme Court has, however, decided that courts must consider the assessments of this overview as decisive reference when it comes to determine whether pharmacies from other EU as well as from EEA countries may undertake mail order trade in medicinal products towards Germany.**

Starting from the premise that comparable does not mean identical and that, in other countries, regulations or administrative provisions may also be relevant, **the key criterion in this study was that these safety standards comply with the judgement of the European Court of Justice (ECJ) on the case of DocMorris (case C-322/01) and ensure the safety of medicinal products and proper pharmacy services.** Thus, the overview is based on exclusively health-relevant safety standards. These are:

1. Simultaneous operation of a mail order pharmacy and a community pharmacy (*Präsenzapotheke*)

2. A quality assurance programme ensuring
 - a) proper packaging, transport and delivery,
 - b) delivery to the person placing the order or a person designated by him/her,
 - c) the warning that people should consult their GP in case of any health problems,
 3. Supply of registered medicines
 4. Counselling by pharmaceutical staff members in German language
 5. Risk reporting system (e.g. by including a note on websites on how risks related to medicinal products can best be reported)
 6. Consignment tracking system.
- 3.20 The DocMorris case had implied that it would be against EU law to prevent mail order sales of non-prescription medicines. This created some obvious risks to health, to which the German Government had responded by defining regulations to apply to such businesses. It wished to know whether or not sales from other EU/EEA countries or Switzerland were intended to be subject to safeguards of equivalent standard.
- 3.21 Seeberg-Elferfeldt's overview showed that only in the Netherlands and in the UK were standards applied that were regarded as comparable to those the German Government decided were necessary to comply with the DocMorris judgment. Similar standards were expected to be applied shortly in Iceland.
- 3.22 The following table summarises our understanding of the position in each country. Were it not for the judgment in the DocMorris case many governments would chose not to allow medicines to be sold by mail order (as was also indicated by the summary of the earlier position in Table 1), and even after the judgment many have not yet fallen into line.

Table3.2: Mail order in medicines - legal position (actual or planned) 2007

Prohibited – all medicines	Permitted – all medicines	Permitted – non-prescription medicines only	Permitted – with safety standards equivalent to those believed by German Government to be required by DocMorris judgment	Permitted – with possibly lower safety standards
Austria				
		Belgium		Belgium
		Bulgaria		Bulgaria
Cyprus				
	Czech Republic			Czech Republic
	Denmark			Denmark
Estonia				
	Finland			Finland
		France		
	Germany		Germany	
Greece				
		Hungary		Hungary
	Iceland		Iceland (from 2008)	
		Ireland		Ireland
Italy				
		Latvia		Latvia
Liechtenstein				
	Lithuania			
Luxembourg				
Malta				
	Netherlands		Netherlands (in part)	
Norway				
		Poland		Poland
Portugal				
	Romania			Romania
Slovakia				
	Slovenia			Slovenia
		Spain		Spain
Sweden [de facto]				
Switzerland				
	UK		UK	

Source: Europe Economics interpretation of report by Dr Niels-J Seeberg-Elferfeldt, Dec 2007

The DocMorris Case (C-322-01)

- 3.23 DocMorris is a pharmacist based in the Netherlands that advertises (and had been very successful in selling) all kinds of medicines by mail order to customers including in Germany.⁹
- 3.24 A case was brought against the company by the Apothekerverband, representing the interests of German pharmacists, and the German court referred some questions to the ECJ. In its ruling in December 2003 the ECJ said in effect that:
- (a) A distinction should be drawn between prescription medicines and pharmacist medicines (non-prescription medicines that may nonetheless be legally supplied only through a registered pharmacist).
 - (b) Community law allows a national Government to ban mail order sales of prescription medicines, but does not require it to do so.
 - (c) On the other hand, Community law would prevent the banning of mail order sales of non-prescription medicines including those that can under national legislation only be purchased from a pharmacist.
 - (d) It makes no difference whether the products are re-imports (parallel trade).
 - (e) The law about advertising medicines to the public applies to mail order pharmacists in the same way as to others. Non-prescription medicines can be advertised, but prescription medicines cannot.
- 3.25 There follows an excerpt from the Judgement of the Court on the case Doc Morris vs. Deutscher Apothekerverband on 11 December 2003 (emphasis added).

3.26 THE COURT,

in answer to the questions referred to it by the Landgericht Frankfurt am Main by order of 10 August 2001, hereby rules:

1 (a) A national prohibition on the sale by mail order of medicinal products the sale of which is restricted to pharmacies in the Member State concerned, such as the prohibition laid down in Paragraph 43(1) of the Arzneimittelgesetz (Law on medicinal products) in the version of 7 September 1998, is a measure having an effect equivalent to a quantitative restriction for the purposes of Article 28 EC.

(b) Article 30 EC may be relied on to justify a national prohibition on the sale by mail order of medicinal products which may be sold only in pharmacies in the

⁹ DocMorris was also involved in other litigation, including over the role of pharmacists, and is now owned by Celesio, a large German-based international company. However these developments are largely irrelevant to present purposes.

Member State concerned in so far as the prohibition covers medicinal products subject to prescription. However, Article 30 EC cannot be relied on to justify an absolute prohibition on the sale by mail order of medicinal products which are not subject to prescription in the Member State concerned.

(c) Questions 1(a) and 1(b) do not need to be assessed differently where medicinal products are imported into a Member State in which they are authorised, having been previously obtained by a pharmacy in another Member State from a wholesaler in the importing Member State.

2. Article 88(1) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use **precludes a national prohibition on advertising the sale by mail order of medicinal products which may be supplied only in pharmacies in the Member State concerned**, such as the prohibition laid down in Paragraph 8(1) of the Heilmittelwerbegesetz (Law on the advertising of medicinal products), **in so far as the prohibition covers medicinal products which are not subject to prescription.**

3.27 In a subsequent 2007 case in Germany the Frankfurt District Court decided that DocMorris could sell prescription-only medicines via the internet where medicine corresponded to medicines already available in German pharmacies and were accompanied by appropriate labelling and patient information leaflet.¹⁰

Issues for consideration

3.28 The object of this paper is to consider the issue of possible harmonised provisions in pharmaceutical legislation for internet trade with pharmaceuticals. This can be analysed as follows:

- (a) What are the risks of on-line sales by pharmacies?
- (b) Is there a need for more harmonised Community legislation?
- (c) If so, what should be its content?

The risks of on-line sales by pharmacies

3.29 The risks (confirmed by the Markmonitor study summarised above) include:

- The vendor holding himself out to be a legitimate pharmacy may in fact be a criminal selling counterfeits

¹⁰ Source: Article by George Pickering, Reed Smith Richards Butler LLP 2007

- The purchaser may need face-to-face advice from a qualified pharmacist on how to use the medicines, but cannot receive such advice.
- The online sales may undermine the economic viability of registered pharmacists, whose role may be seen as part of the national infrastructure of healthcare professionals.

The need for harmonised legislation

- 3.30 The result of the DocMorris ruling appears to be that Member States may no longer be able to decide whether or not medicines other than prescription medicines can be sold by internet / mail order. On the other hand, they are not prevented from making their own decisions with regard to prescription medicines, so that it is likely that different arrangements will continue to prevail.
- 3.31 There are perhaps three bases on which harmonisation (meaning in this context standardised laws in each Member State) might be proposed:
- (a) The present arrangements, in which practices differ significantly between Member States, may distort intra-community trade.
 - (b) The present arrangements in many Member States imply a broad variability or even inconsistent approaches on the implementation of the ECJ DocMorris ruling in 2003
 - (c) It might also be argued that the present arrangements in some Member States could have impacts to patient safety.

What might be the content of any new EU legislation in this area?

- 3.32 If it is felt that the legal position following the DocMorris ruling is unsatisfactory, there are a number of policy options that might be considered:
- (a) Legislation based on the DocMorris ruling that would allow but not require Member States to prohibit the mail order/internet sale of prescription medicines but not allow them to prohibit the sales of any other medicines. This would underline the DocMorris ruling but not change its substance. It is therefore not clear that a new EU law of this sort would achieve anything. However it would constitute a change of the current paradigm, which leaves Community rules and legislation on distribution of medicines to the patients by pharmacies and retailers to the subsidiarity of Member States.
 - (b) Making it obligatory for Member States to prohibit mail order supplies of either prescription medicines or all pharmacy medicines.

Commentary

- 3.33 However, the ECJ's DocMorris ruling risks having this effect. Moreover, by making it illegal to prevent the sale over the internet of medicines that, although not prescription medicines, had nonetheless been decided to be safe only for sale by qualified

pharmacists the DocMorris ruling would impose a less secure regime on Member States than their Governments had decided was appropriate. In 2006 23 of 30 European governments (those of the EU Member States and Norway) had decided not to allow e-commerce in medicines; this was the decision of a majority of democratic governments on a matter clearly within their competence.

- 3.34 The ECJ ruling in DocMorris made no attempt to assess the social costs and benefits of the alternative arrangements being considered. This method of analysis pre-dates the EU's adoption of the principle that policy options should be assessed in terms of their likely economic, social and environmental impacts. It is clear that the result of a fuller welfare analysis (using this term to encompass economic, social, environmental and legal issues) in the field of mail order and internet supplies would result in greater weight being placed on patient safety and public health than in a purely legal analysis.
- 3.35 The issue would benefit from an independent study (perhaps conducted by a group representing European Pharmacists) that fully identifies and quantifies the risks involved with on-line pharmacists and the advantages and disadvantages should they be barred from conducting business in the EU/EEA.
- 3.36 This raises a much larger question – also brought forward by the analysis in other parts of this research into the ECJ judgements in cases bearing on trade in pharmaceuticals – of how in the future the ECJ should take account of economic and social (including healthcare) issues in the area in which healthcare and trade policies intersect.

APPENDIX 1: CLINICAL TRIALS

Introduction

3.37 The brief for this stock-taking report is to:

Review import, manufacturing and distribution requirements for clinical trial medication with a view to prevent counterfeiting.

3.38 This report is one of four required from Europe Economics to complete Specific Contract No S12 446433 under contract ENTR 04/093 LOT 4, following the urgent work in April and May 2008.

3.39 The resource available is limited by the contract, and it would not be proportionate for to carry out in-depth study such as we have made of previous issues. The present report is thus seen as a “stock-taking” exercise, the conclusions of which would be the identification of issues for consideration. A length of 3-5 pages should suffice.

Requirements to prevent counterfeit medicines in clinical trial directive 2001/20/EC and 2005/28/EC.

3.40 These Directives lay down detailed administrative procedures which MS are obliged to follow in clinical trials, including such matters as the ethical standards to be followed and the qualifications of inspectors.

3.41 The Commission is aware of a report of counterfeit Plavix in a UK clinical trial; this was mentioned in the UK fact-finding mission report (2007) as follows:

Q. Are there any improvements not covered by previous questions that you would like to see made to the present system? Please substantiate any social, economic and environmental impacts if possible.

A. Medicines used for clinical trials are excluded from certain provisions for other medicines in Clinical Trial Directive 2001/20/EC: import provisions are different from "regular" medicines, e.g. medicines can be purchased from anywhere without requirement on retesting. These exemptions also apply to the comparator product (which may be a licensed drug already marketed). Companies may import such products (under lower import requirements) for clinical trials but finally do not sell them for clinical trial purposes but for the regular distribution chain (e.g. wholesalers, pharmacies).

Example: Plavix (Jan 2007): German wholesaler bought (counterfeit) from outside EU and then sold to UK wholesaler for clinical trails;

Without changing Directive 2001/20/EC Annex 13 could be reviewed to amend obligations for the Qualified Person in this regard.

In addition, the RAS system does not involve clinical trials – needs to be considered in the future.

- 3.42 A subsequent episode of counterfeit Plavix was recorded when, in May 2007 the MHRA issued a Drug Alert to recall parallel distributed Clopidogrel tablets 75mg marketed as Plavix in France by sanofi-aventis and BMS in French livery. The EMEA was notified by over 30 parallel distributors to sell these products into the UK, and some of the supplies were counterfeit. EMEA could not tell MHRA which were the firms concerned and MHR had to issue a general alert (action in six hours, including out of office hours) to recall the products.
- 3.43 It is not on record whether the two incidents were related but this is clearly a possibility to which MHRA drew attention in the fact-finding mission interview.

Legal background

- 3.44 Directive 2001/20/EC is intended to ensure that high standards of safety (and high ethical standards) are observed in clinical trials. Paragraph 15 of the preamble states that:

The verification of compliance with the standards of good clinical practice and the need to subject data, information and documents to inspection in order to confirm that they have been properly generated, recorded and reported are essential in order to justify the involvement of human subjects in clinical trials.

- 3.45 Article 13 of the Directive deals with the manufacture and import of investigational medicinal products. It requires Member States to “take all appropriate measures to ensure that the manufacture or importation of investigational medicinal products is subject to the holding of authorisation that shall meet at least requirements defined by the Standing Committee on Medicinal Products for Human Use”.
- 3.46 The Directive refers to Annex 13 of the GMP Guidelines (July 2003) which details procedures to be followed including with regard to quality control (on the basis that since processes may not be standardised or fully validated testing takes on more importance in ensuring that each batch meets its specification (paragraph 34)) and to the release of batches (e.g. paragraph 40).
- 3.47 Directive 2005/28/EC adds to Directive 2001/20/EC by expanding on the duties of inspectors, and by adding to the details of how ‘research and development’ trials should be conducted (Article 3(3) of Directive 2001/83/EC having made clear that the requirements applying to commercial clinical trials do not apply to research and development trials).
- 3.48 It is thus clear that:
- (a) The relevant Directives recognise the particular importance of high safety standards in clinical trials; and
 - (b) that within complex legislation there are possible gaps with regard to import and distribution of products for use in clinical trials.

Comment: policy options for consideration

- 3.49 Directives 2001/20/EC and Directive 2005/28/EC both rely on the idea that safety can be ensured through adherence to GMP. Neither refers to the particular problems of counterfeits.
- 3.50 It appears from the work done in other parts of this project that the risk of counterfeits is a distinct issue from the question of general manufacturing standards, and that better compliance by legitimate manufacturers with GMP principles, although desirable in itself, is not directly relevant to the objective of combating counterfeits. It is also clear that the lack of transparency throughout the distribution chain creates conditions in which the risk of counterfeits is greater than it would be if the supply chain were transparent, and that the lack of transparency is largely the result of parallel trade (sometimes referred to as the 'grey market'.)
- 3.51 Among the recommendations for policies to combat counterfeits were suggestions to exclude from the scope of parallel trade products recognised as particularly high risk. At that stage, the issue of clinical trials had not been reviewed; but the risks for the public if counterfeit medicines are used in clinical trials can be tremendous. If an authorisation is based on clinical trials in which the comparator products had no or a low level of active ingredient, the assumptions made on the safety and efficacy of a new product made with the authorisation could be misleading. This could have effects on thousands of patients.
- 3.52 The concerns equally apply to commercial and to research and development clinical trials.
- 3.53 If however, for any reason, the Commission is unwilling to limit parallel trade and other measures have to be considered, the MHRA suggestion noted above appears to have merit. If tighter controls can be achieved through tightening the responsibilities of inspectors under the GMP requirements, this should be considered.
- 3.54 Consideration should also be given to further tightening of provisions for the import and wholesale distribution of products to be used in clinical trials. Measures with respect to ensuring products are bought from secure sources (e.g. audits) as currently discussed for products placed on the market should correspondingly considered for clinical trials.

APPENDIX 2: TRACK AND TRACE TECHNOLOGY

Stocktaking and State of Play of various Track & Trace Technologies

- 3.55 This report is one of four required from Europe Economics to complete Specific Contract No S12 446433 under contract ENTR 04/093 LOT 4, following more urgent and higher priority work in April and May 2008. This contract is for research into the likely impacts of policies designed to reduce the risks of counterfeit medicines and of unsafe medicines being delivered through parallel trade.
- 3.56 DG Enterprise accepts that the resource available must be limited, and that it would not be proportionate to require an in-depth study such Europe Economics has previously made of other issues under this contract. The four reports are seen as “stock-taking” exercises, the conclusions of which would be the identification of gaps in what is known and issues for possible further work by DG Enterprise and Industry rather than policy recommendations. If they can be done quickly, DG Enterprise will be happy to expedite the administration so that payment can be made for the completion of the contract.
- 3.57 The report reviews a number of published sources of information on this subject. Unless otherwise stated the views expressed in this report are those of the authors of the work reviewed rather than of Europe Economics.
- 3.58 No firm overall conclusions are drawn from this review, but:
- (a) With regard to prescription medicines supplied through the conventional legitimate chain, it appears that there is already a wealth of technological devices that would allow individual packs of medicine to be tracked from manufacturer to the pharmacist or medical professional supplying the patient. Opinion is still divided on whether 2D bar codes or RFID devices are more appropriate for general use.
 - (b) With regard to other medicines, including those sold over the internet or OTC from pharmacists or other retail outlets, there is not yet any obviously feasible way of allowing customers to use track & trace technology to help to detect counterfeits.
- 3.59 Assuming that is clearly desirable that there should be the possibility of checking the authenticity of medicines, particularly prescription medicines, before they are taken by patients the policy issues for consideration by DG Enterprise and Industry might be:
- (a) Whether or not it would be appropriate for the authorities to mandate a technology to be used for this purpose. In theory, a standard system might reduce industry costs and be most consistent with a standardised approach throughout the EU single market; such an approach might be supported by the major manufacturers. On the other hand, it would draw government officials, including the Commission services, into a position in which they had to take a view on alternative technologies. There are strong economic arguments in favour of allowing competition between alternative technologies, and for limiting the role of the state to setting necessary minimum standards.

(b) Whether any standard setting in this area is a matter best decided at EU or national level.

3.60 The material reviewed in this report is divided into three parts: some assessments by some government or international agencies; assessments by some market participants and technology suppliers; and assessments by some businesses involved in the supply chain.

Some Official Assessments

WHO 2006 (CONFIDENTIAL)

3.61 A confidential World Health Organisation (WHO) report in 2006 discussed anti-counterfeit technology for the protection of medicines.

3.62 Technologies are classified as overt, covert, forensic and “track & trace”. Each category is described, pros and cons analysed and conclusions derived.

3.63 Overt features should be used at discretion of manufacturers, especially for products “at risk”, not mandated by authorities. Covert solutions by manufacturers should be encouraged across the whole range of products, as they tend to be beneficial with respect to limited costs. Use of forensic markers by manufacturers should be encouraged for products at high risk.

3.64 Track & trace tagging should command investment by manufacturers and healthcare providers. RFID is possibly the long term solution, but interim solutions should be established.

WHO 2007

3.65 In a report “Anti-counterfeit Technologies for the Protection of Medicines” published by the WHO in 2007 the author, Geoff Power, proposed a similar categorisation of technologies to combat counterfeits to that suggested by the WHO in the previous year. His discussion is summarised as follows:

Overt systems:

3.66 Anti-counterfeit technologies would ideally allow the public to check that goods were genuine. Overt systems are visible to end users who may be able to check authenticity, and expensive for the counterfeiter to reproduce, but on the other hand they may add significant cost to the manufacture, and it may be necessary to educate the users to their recognition.

3.67 Overt systems include holograms, optically variable devices (OVD), and colour shifting security inks and films. (Sequential numbering is vulnerable because the sequence may be predictable and easily replicated. It is necessary to add a database check and a random element.)

- 3.68 There is a danger that devices used in overt systems could be re-used if they are not destroyed properly after the medicine had been consumed. Other disadvantages are that they may provide false assurance and they can be vulnerable to an imperfect copy by the counterfeiter.

Covert systems:

- 3.69 Covert systems include invisible ink, embedded image, and digital watermarks. They are low cost and 'regulator free' so can be changed quickly but need secrecy to work.
- 3.70 Covert systems lose their value if they are known about by counterfeiters; they can be reproduced but can only be detected by specialists (those who know basic identification techniques).

Forensic markers:

- 3.71 Forensic markers need scientific checks to validate (e.g. biological, chemical or DNA taggants). They are secure but costly to implement.

Track and trace:

- 3.72 Track and trace devices can be used to check the identity of products at different points in the supply chain and to provide an e-pedigree that can be authenticated at any time. Their use can reduce medication errors and lead to more effective recalls.
- 3.73 Serialisation of packs involves allocating a random number so that, although the packs can be copied, comparing the number to a database will identify invalid or duplicate numbers (there needs to be careful restriction of database access).
- 3.74 Bar codes are about 1cm square for 2D or can be linear if there is sufficient space. They can contain about 1Kb of data with 'redundancy' or error correction. An entry on a case can be linked to the contents it should have.
- 3.75 RFID can be interrogated at a distance without line of sight, and has the potential to be fully automated in warehouses through to pharmacies without manual intervention (including possibly remote scanning). In some circumstances such as hospitals they could eliminate dispensing errors, facilitate recall and reduce stock expiry.
- 3.76 Problems with this technique include the tag and scanner cost, the robustness through to end of life with a significant failure rate currently experienced, and concerns over privacy or tampering of the tags. The costs of RFID are not affordable for generics or over the counter medicines.

Table 5.1: Track and trace Advantages (left) and Disadvantages (from report)

High tech and secure against copying	Significant cost to implement and monitor
May be capable of remote authentication, via phone or internet	Difficult to implement across multiple markets
May be accessible to authorities and investigators without compromise	May be vulnerable to hackers
May eliminate dispensing errors	Damaged labels may not read
Facilitates recall of defective product	Robustness of RFID tags not proven
May combat theft and fraud	Needs harmonisation of standards
Benefits in supply efficiencies	Not accessible to the public
	Remote reading causes privacy issue

- 3.77 In the view of the authors of the report, there would be little use in mandating that an overt feature was included in medicine packets, because counterfeiters will defeat or circumvent this. Covert measures should be used sparingly and secretly though could be shared with some trusted supply-chain partners. Forensic measures can be suitable for very expensive products and then it can be cost-effective to spread them to others. Track and trace features can be copied but a common database can be used to support several technologies such as 2D barcode and RFID.
- 3.78 For speed and economy a barcode system should be developed and RFID should be added when feasible. RFID is more effective at the pallet and case level, but 2D barcode is affordable at the pack level. An industry group should be formed to define standards consisting of representatives from branded and generic manufacturers, distributors, pharmacists, healthcare professionals, and customs, police and patients. As well as product integrity, this could help supply chain efficiencies and reduce the amount of expired stock.

FDA 2004

- 3.79 The US Food and Drugs Authority (FDA) Counterfeiting Drug Task Force was created in 2003 and collected extensive comments by security experts, enforcement officials, technology developers, manufacturers, wholesalers, retailers, consumer groups and the general public. It produced a report in 2004 “Combating Counterfeit Drugs”.
- 3.80 The FDA approach to combating counterfeits has been based on:
- (a) Rapid adoption of new technologies to protect the drug supply, including RFID and authentication technologies. Adoption of electronic track and trace technologies.
 - (b) Strong anti-counterfeit laws and increased criminal penalties.
 - (c) Adoption of secure business practices by all participants in the supply chain. Effective reporting system strengthening FDA’s response.
 - (d) Education of both consumers and professionals about the risks of counterfeit drugs and how to protect against such risks.

- (e) International collaboration among stakeholders to develop common strategies and deter and detect counterfeit drugs globally.

FDA: 2006 Update of 2004 Report

- 3.81 The FDA admits that the goals of traceability can be achieved by using 2-D barcodes instead of more complex RFID (Radio Frequency Identification), and that a hybrid paper-electronic environment is the most feasible option, at least in the short-term.
- 3.82 There has been a failure of widespread adoption of RFID. The reasons cited include: lack of standards, privacy concerns, challenges in serializing all products, concerns about ownership of confidential business transaction data, concerns over accuracy and speed of electronic devices and systems, lack of data on how radio signals affect sensitive products.
- 3.83 The FDA suggests a “phased in” approach where RFID is first rolled out to drugs with high sales volume and high risk of being counterfeited.

FDA: Prescription Drug Marketing Act Pedigree Requirements¹¹

- 3.84 The FDA notes that:

“Section 503(e)(1)(A) of the act establishes the so-called “pedigree” requirement for prescription drugs. A drug pedigree is a statement of origin that identifies each prior sale, purchase, or trade of a drug, including the dates of those transactions and the names and addresses of all parties to them. Under the pedigree requirement, each person who is engaged in the wholesale distribution of a prescription drug in interstate commerce, who is not the manufacturer or an authorized distributor of record for that drug, must provide to the person who receives the drug a pedigree for that drug. The PDMA states that an authorized distributor of record is a wholesaler that has an “ongoing relationship” with a manufacturer to distribute that manufacturer’s drug. However, the PDMA does not define “ongoing relationship.””

“Today, the agency is announcing that it does not intend to delay the effective date of Sec. 203.3(u) and 203.50 beyond December 1, 2006. As such, these provisions defining “ongoing relationship” and setting forth requirements regarding the information that must appear in pedigrees will go into effect as of December 1, 2006.”

- 3.85 In February 2004 the FDA introduced bar code labelling requirements for human drug products that enforced the inclusion of bar codes on most prescription drugs.
- 3.86 Some states have gone further than this federal legislation, e.g. California was the first to demand an electronic drug pedigree. While Florida and Indiana laws focus on the distribution chain, beginning with the wholesaler, California became the first state to

¹¹ <http://www.fda.gov/OHRMS/DOCKETS/98fr/06-5362.htm>

mandate that the pedigree documents be initiated by the manufacturer, and so bears the most relevance for pharmaceutical manufacturers. A stay in enforcement has been granted, but from January 2009 manufacturers will be required to provide a pedigree to any wholesaler or pharmacy acquiring a drug that is shipped into the state of California. (The original implementation date was set when it was thought that a national RFID system would be in place by 2007, but subsequently national implementation date was delayed.) The FDA seems to favour a harmonized numbering scheme for mass serialization but has not yet resolved implementation issues.¹²

- 3.87 **FDA Pedigree** requires 10 items: each prior transaction, lot numbers, number of containers, business name, proprietary name, business address, established name, date of transaction, strength, container size.¹³
- 3.88 **Florida Pedigree** requires seven items: amount of drug, dosage and strength, lot numbers, name and address of each owner of legend drug and signature of owner, signed shipping information, invoice number, or unique number identifying the transaction, certification that recipient wholesaler has authenticated pedigree process
- 3.89 **California Pedigree** is defined as: Electronic record, containing information regarding each transaction resulting in a change of ownership of a prescription drug, from sale by manufacturer, through acquisition and sale by a wholesaler, until final sale to a pharmacy or person furnishing, administering or dispensing the prescription drug. Requirements are: prescription drug information, transaction and source information, ownership information, and certification, but there are doubts in 2008 about whether this is feasible.

DG INFOSOC: public consultation 2006

- 3.90 This is a substantial write-up by DG Information Society and Media in September 2006 of the results of about 2000 replies, 70 per cent from individuals, to an on-line public consultation about RFIDs, entitled: 'The RFID Revolution: Your voice on the Challenges, Opportunities and Threats'.
- 3.91 The replies suggested that there might be substantial concern from individuals about threat to privacy from RFIDs (people did not want to be tracked and traced from things they were wearing or carrying, particularly by employers). There were generally divided views about RFIDs and what role governments or the EC should be expected to play.

¹² Based on EC fact-finding mission to US. the FDA was set to begin enforcement in December 2006 but was blocked by a court injunction. This has left the program in limbo until end 2007 and possibly until state measures come into effect, with the first planned in California on 1/1/2009 and later in Florida and Nevada. US pharmaceutical companies have tended to delay the introduction of these rules as they do not see the added value but fear the additional effort. Rules on pedigree were originally planned to be introduced in 2000, but the speed of adoption may increase now with the coming federal legislation. As indicated, California requires an RFID.

¹³ http://www.neu.ceedutest.com/ce_dpl/DPL_handout.pdf,
<http://www.maxiomgroup.com/pdf/pubs/MaxiomGroupNJLifeSciTechPedigreeArticle.pdf?idSeccion=450>

DG INFOSOC 2007

3.92 This material refers to the draft final report (v31112007) of an impact assessment by DG Information Society and Media on how to implement RFID and still maintain privacy principles. It contains some information relevant to the present stock-taking.

RFID: key characteristics

3.93 Radio Frequency Identification (RFID) is the designation for a microchip technology that uses radio signals to automatically identify goods, vehicles, animals and people. The basic components of an RFID system are a tag (a transponder), which is attached to an object, a reader (sometimes called an interrogator) which is able to retrieve data from the tag and middleware to link RFID-data with the ICT infrastructure and application tool of the user. The tag and the RFID receiver communicate with each other via a radio link.

3.94 As with all other IT systems, RFID systems can vary in terms of complexity and implementation. The following common subsystem building-blocks can be distinguished:

- (a) The RF subsystem (front end-system). This subsystem consists of the RFID tag and the RFID reader and is the part that performs identification and related transactions over a wireless interface.
- (b) The enterprise subsystem. This subsystem comprises the computers and software necessary to process and store data acquired from the RF subsystem.
- (c) The inter-enterprise subsystem. This subsystem is used to connect different enterprise subsystems to each other if information needs to be shared between organisations.

3.95 The comment is made that implementing an EU-wide RFID may be expensive, both in fixed and running costs.

Active and passive tags

3.96 RFID tags can be passive or active. Passive tags do not have their own power source and need to be activated by the reader's field which charges the tag. This typically requires a stronger field and makes these tags more suitable for short read-range applications. This type of tag is relatively cheap, light, and compact.

3.97 Active tags are powered by their own battery and can emit a detectable signal. Their lifetime is determined by their battery. These tags often have read and write capacities and increased memory capacity. These tags are relatively larger and more expensive.

3.98 Different parts of the frequency spectrum are assigned to different purposes by government regulation. A multitude of frequency bands are in use for RFID, divided into four groups: Low Frequency (LF), High Frequency (HF), Ultra-High Frequency (UHF), and Microwave. The table contains the frequency and read ranges.

Table 5.2: Frequency bands and application

	LF	HF	UHF	Microwave
Frequency Range	< 135 KHz	10 – 13.56 MHz	860 – 960 MHz	2.4 – 5.8 GHz
Read Range	~10 cm	~1 m	2 ~ 5 m	~100 m
Coupling	Magnetic, Electric	Magnetic, Electric	Electromagnetic	Electromagnetic
Application	Smart Card, Ticketing, Anti-Theft, Animal Tagging	Small Item Management, Anti-Theft, Supply Chain	Transportation, Vehicle ID, Access/Security, Large Item Management, Supply Chain	Transportation, Vehicle ID, Access/Security, UWB Localisation

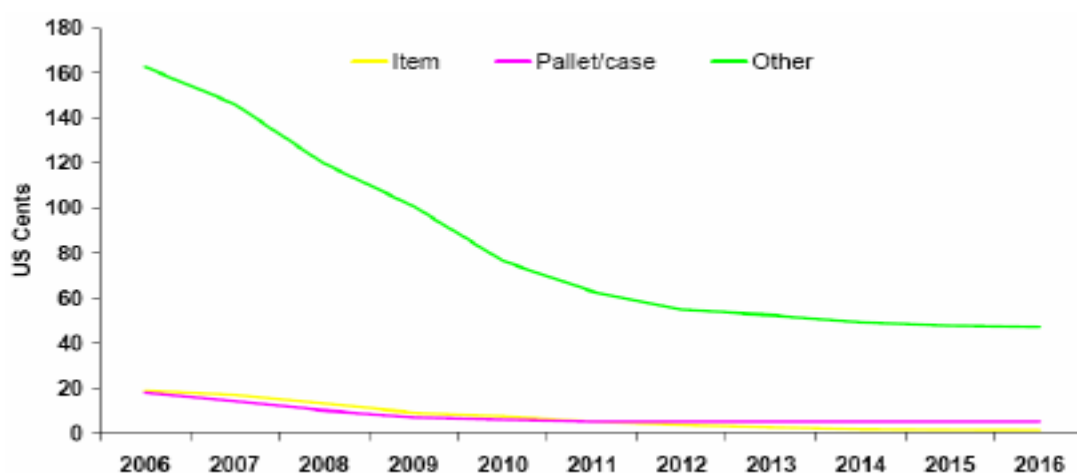
Unique number

3.99 Sometimes RFID is considered the replacement of the barcode. A major difference between an RFID and a barcode is the numbering used for RFID. Barcodes can have the same number for an entire product range. When using RFID, each product will contain a RFID tag with a unique number so every item can be uniquely identified.

Cost

3.100 In 2007 the price for the cheapest tags was around €0.14-€0.18 per tag. Cost reductions are foreseen with tag prices expected to drop to €0.04 within a few years. About half the RFID market is accounted for by the market for tags (other revenues are for software, consultancy services, and scanners).

Chart A5.1: Expected average price tag per application (2006-2016)



Source: IDTechEx

3.101 There are public concerns that RFID may lead to privacy breaches. Information security is another potential worry.

- 3.102 The possibility of linking the collected information directly or indirectly to persons is one of the main areas of concern, especially with respect to item level tagging at the consumer or patient level.
- 3.103 RFID in principle introduces the possibility to track and trace people's movements, establish profiles (e.g. on purchasing behaviour) or misuse personal data stored on the RFID tags or in the database (this risk does not apply to barcodes that cannot be read remotely). This risk does not always materialise from the introduction of RFIDs alone (which do not always contain personal ID data themselves) but can arise by combining several information sources or combining database information. The privacy issue could also cause problems at an EU level, with different Member States having different views and policies.

European Commission: Decision on UHF Spectrum Harmonisation November 2006

- 3.104 The EC Decision on UHF Spectrum Harmonisation, 23 November 2006, is designed to facilitate the introduction of RFIDs, particularly passive devices that do not have their own power sources. Within six months of implementation of the Decision, Member States are obliged to 'designate and make available' the frequency bands for RFID laid down in the Annex to the Decision .

EU Member States / EEA Survey.¹⁴

- 3.105 Some EEA countries do have requirements to track products back to suppliers, however in some countries these requirements are restricted to veterinary products and in others there are no requirements or batch numbers are not required.

¹⁴ From Member States survey conducted by Commission in 2007.

Table 5.3: Tracking & Tracing in the EU

Member state	Are there any specific regulatory requirements for tracking and tracing medicines in your member state from manufacturers to patient distribution?
Austria	No
Belgium	Not clear
Bulgaria	No questionnaire received
Czech Republic	No questionnaire received
Cyprus	Wholesalers have to maintain records of traceability of the products they procure and distribute.
Denmark	No questionnaire received
Estonia	Yes, wholesalers can only accept products from suppliers on the basis of consignment documents and are obliged to notify the Agency about cross-border sales of notational medicinal products, including importer/exporter. Dispensing from pharmacies naturally can be traced back only in case of prescription only products.
Finland	Yes, wholesalers must keep records of imports, procurement, storage and sale of medicinal products.
France	Yes (legislation is expanded in the full response)
Germany	No. However, there is an obligation to track and trace deliveries from a mail order pharmacy to consumer or patient.
Greece	No questionnaire received
Ireland	Not clear. Regulation specifies that only holders of licenses may sell veterinary medicines and requirements for veterinary practitioners and pharmacists to keep records and farmers.
Italy (Veterinary)	Yes (from 2008) there will be a bar code system for the tracking and tracing of commercialised veterinary medicinal products.
Latvia	Not clear, (legislation is explained in the full response)
Liechtenstein	No clear. Under the GMP guide and the Good Distribution Practice manufactures and distributors have to have a system in place by which the products can be traced.
Lithuania (Human)	Yes, according to the Good Manufacturing practice rules in respect of medicinal products and investigational medicinal products.
Lithuania (Veterinary)	Requirements for Manufacture, Authorization and Marketing of Veterinary Medicinal Products in the Republic of Lithuania (O.G., 2005, No. 131-4754) (Law is expanded)
Luxembourg	No questionnaire received
Malta	No provisions like specific labelling are in force. (law is expanded in the full response)
Netherlands	Yes. From manufacturer to wholesaler the batch number must be recorded. From wholesaler to pharmacy this is done on a number of companies.
Norway	Yes. At the pre-wholesale level there is a requirement for track and trace systems for specific batches, but not at the patient level.
Portugal	Have transposed the GDP approved in Directive 92/25/EC.
Poland	No questionnaire received
Romania	Not clear. Regulatory requirements for the distribution of medicinal products have been established by the Ministry of Health (law is expanded in the full response).
Slovakia (Veterinary)	Act 140/1998 Coll. (law is expanded in the full response)

Slovakia (Human)	Section 30 (1)d), section33(1) c), Section 36(2) e) of the Act 140/1998 Coll. on medicinal products and medical devices; Order Ministry of Health Slovak Republic No.274/1998 Coll. On GMP a GWP
Slovenia	N/a
Spain	Yes. Under the Law on Guaranties and Rational Use of Medicines and Medical Devices, a tracking system for all medicines, from the manufacturer to the final user.
Sweden	Traceability of batch number including the wholesaler chain is applicable.
UK (Veterinary)	Directive 2001/82/EC requires manufacturers, wholesale dealers and retailers to keep records to enable Veterinary Medicinal Products to be tracked and traced.
UK (Human)	No. However, under Article 80 of Directive 2001/83/EC, as Amended, Title VII, Wholesale distribution, holders of the distribution authorisation must keep records for any transaction to include at least the date, name of the medicinal product, the quantity received/supplied and the name and address of the supplier/consignee.

German fact-finding mission 2007

- 3.106 In a 2007 European Commission fact-finding mission it was found that in Germany pharmaceutical companies are legally required to document to whom they deliver their products. Therefore, they can track batches to their direct customers (wholesalers or pharmacies in case of direct supply). There exists no tracking system that includes all pharmacies.
- 3.107 Currently no specific requirements exist in Germany for track and trace but Germany would be likely to support and encourage introduction of appropriate technology, e.g. 2D bar-coding.
- 3.108 Germany would welcome harmonised technology requirements. An EU wide solution would be preferred to a national solution. Track and trace systems based on appropriate technology, e.g. 2D barcode, should become a mandatory requirement in the EU for all types of product, a view which is supported by a broad range of companies. A differentiated approach concerning product categories would imply a huge burden of costs at each stage of the distribution chain as different systems would have to be installed in parallel. Therefore, requirements should be the same for all types of products, with no differentiated approach for different products or categories of products. Otherwise counterfeiters would move to other products. Even low price products are known to be counterfeited. Germany is concerned about parallel trade activities on technologies, e.g. for advanced therapies and tissues which have recently been launched.
- 3.109 An overview of national wholesalers is kept by using local databases in the single inspectorates. A European database would be beneficial.

UK fact finding mission 2007

- 3.110 Parallel traders use different batch numbering systems than the original manufacturer. In the case of suspect counterfeits a "blanket recall" could be necessary without batch numbers. In such a system a targeted recall is difficult; problems arise if there are

multiple parallel traders. Patient safety issues could arise if in such a case no product was left on the market (such examples exist for generics). An examples where this led to problems was the Plavix recall of counterfeit in parallel trade in 2007.

- 3.111 MHRA does not know how many products have reached the patient in all cases. For Zyprexa and Plavix: together at least 30,000 packs have reached patients; less than 10 packs of Casodex have reached the patients. The MHRA also say that for a combination of other recalls less than 5000 packs for Plavix, Zyprexa, and Casodex have reached patients. The MHRA did not know how much reached pharmacies or hospitals. Information could only be obtained if full traceability (e.g. audit trail) was required. Since batch numbers are not recorded there is a problem that it is difficult to keep track of all products.
- 3.112 A track and trace could resolve the problems, however the UK does not support a rigid policy at this stage. Any EU wide system should be voluntary; if 2D barcode could improve the counterfeit situation then this would result in savings related to frauds. Consideration should be given as to whether manufactures should be made responsible for the infrastructure costs. Current traceability requirements are that firms must maintain a copy of wholesale dealer's license of their suppliers. Non-compliance would constitute a GMP issue, administrative action would be taken. One MHRA member said that the main cause of concern was the 40 per cent of UK licensed wholesalers that are inactive at any one time.
- 3.113 There is no enforcement of traceability (no legal requirement for full traceability). Retail pharmacies buy from manufactures or wholesalers and may sell products back into wholesale distribution chain (this can be a problem where pharmacists return small amounts of sub-standard stock, e.g. near expiry or poorly packaged, rather than the medicine that was delivered by the wholesaler), so there is a problem on how to track this. The effectiveness of cold chain throughout supply chain (involving also parallel trader and pharmacies) may be an issue: To maintain full cold chain traceability a data logger from the manufacturer to pharmacy level (cheap sticker) would be useful.
- 3.114 There has been a shift of counterfeits from lifestyle to life-saving medicines, the most recent case was for Glivac (leukaemia drug) (£1400 per pack). Detection of counterfeits has been increased sharply. Ten years ago no cases were known; enforcement has increased significantly; in this light it is not clear to which extent in fact incidents are increasing. 3-4 FTE investigators are working on cases.
- 3.115 A database of GDP authorisations would require harmonisation of wholesale license format which is currently a barrier or may not be legitimate. A database on counterfeiting incidents is the most important although some information is available through Europol and information must be kept simple to ensure regulators can keep to time constraints. A national database on wholesale license exists, which is public, however a "EudraGDP" and a common format for a wholesale license would be supported. This requires a GDP certificate, so the impact needs to be assessed before the advantage is known.

- 3.116 The UK is probably the only Member State to cooperate with PSI at this point. Ireland is likely to start such cooperation. There is no possibility for a direct database consultation by competent authorities, but MHRA checks with PSI on a case-by-case basis before investigation on an unlicensed company starts.
- 3.117 The links between counterfeiting and organised crime are known to include:
- (a) Tamiflu has been mentioned as potentially targeted by terrorists for counterfeits.
 - (b) Traditional organised crime groups have also started supply of counterfeit medicines (e.g. a traditional cocaine gang now "trades" Viagra in addition).
 - (c) Money laundering: "Stormgand case" (investigation, bank accounts; main products: Cialis, Propecia, Reductil).
 - (d) Criminals take advantage of the gaps; make contact via Business to Business websites.
- 3.118 Medicines used for clinical trials are excluded from certain provisions for other medicines in Clinical Trial Directive 2001/20/EC: import provisions are different from "regular" medicines, e.g. medicines can be purchased from anywhere without requirement on retesting. These exemptions also apply to the comparator product (which may be a licensed drug already marketed). A company may import such products (under lower import requirements) for clinical trials but finally do not sell them for clinical trial purposes but for the regular distribution chain (e.g. wholesalers, pharmacies). For Example: Plavix (Jan 2007): German wholesaler bought (counterfeit) from outside EU and then sold to UK wholesaler for clinical trails. Without changing Directive 2001/20/EC Annex 13 could be reviewed to amend obligations for the Qualified Person in this regard. The RAS (rapid alert) system does not involve clinical trials, so this needs to be considered in the future.

The Belgian situation September 2007

- 3.119 A unique barcode has to appear on all reimbursed medicines that are brought on to the market. This consists of a CNK (7 digits), packet ID (8 digits) and a check or control digit. The number appears underneath the barcode. A packet can only be charged to reimbursement once preventing reimbursement fraud. Mass serialization to prevent reimbursement fraud was started in 2004 and on-line authentication in 2006. No interference with work-flow as fully integrated. No investment cost as only requires existing barcode reader. Database considers barcodes, expiry dates and recalls.

Security Technology Firms and Market Participants

GIRP

- 3.120 GIRP is the trade association representing full-line wholesalers.

- 3.121 GIRP supports the development of a harmonised track & trace system in the EU. It believes that it will be absolutely necessary to have national product identification, and batch number and expiry date in machine readable format.
- 3.122 With regard to the technology, it thinks that a 1-D bar code would be either incomplete or too big, and doubts whether RFID is yet a 'mature technology'. It favours 2-D bar codes as able to include all information needed and notes that additional information useful to the industry can be saved.

RFID Byline, RFGlobalnet

- 3.123 RFGlobalnet is an internet site advertising products and services related to RFID. Some points of interest are:
- (a) It is possible to implement RFID including a 'destroy' command to protect patient privacy after the point of sale.
 - (b) RFID could reduce overstocking and expired stock which currently cost the industry \$2bn a year.
 - (c) Hospitals could reduce operational overheads by tracking products and further savings would be made by tracking patients.
 - (d) RFID tags (NXP ICODE) can be made with one-time unique programmable memory to prevent tampering.

www.vardexlaser.com , August 2007

- 3.124 The Vardex Laser Corporation (Vardelexer) advertises a 'Combination Product Authentication and Mass Serialization Track And Trace System Low cost-effective, state-of-the-art pharmaceutical anti-counterfeiting solution!'
- 3.125 This system, the VDL, is claimed to be a cost effective and reliable approach for coding pharmaceutical products from single piece (i.e. capsules and tablets) through unit-of-use packaging (i.e., labels, bottles and boxes). It offers a unique pattern that does not add nor change the chemical composition of the product, and a high-speed coding process. It provides definitive proof of each product's validity through verification via a secured database using scanners and readers. Tablets can be linked to the unit of use, which can be linked to the case and the pallet. Drug pedigree is recorded electronically and kept up to date through the supply chain. A prototype was introduced May 2007.

Table 5.4: VDL comparisons

Comparison of the VDL to Leading Pharma Anti-counterfeiting Technologies				
	VDL	RFID	Scanner Laser	Inkjet Printing
Codex Type	Dot Matrix Images Barcode	Not Applicable (Uses Tags)	Barcode	Barcode Dot Matrix
System Size	✓ Small	Large	✓ Small	✓ Small
Coding Speed	✓ Fast +	Slow	Slow	Slow
Coding Security	✓ High +	✓ High	Low	Low
Process Security	✓ High	✓ High	Low	Low
Different Materials	✓ Many	✓ Many	✓ Many	Limited
Lowest Level of Coding	✓ Piece	Unit	Unit	Unit
Tracking Effort	Medium	✓ Low	Medium	Medium
Reliability @ Unit Level	✓ High	Low	✓ High	✓ High
System Cost	✓ Low	High +	✓ Low	✓ Low
Operating Cost	✓ Low	High +	✓ Low	High

Briefing Paper on Authentix, Inc.

3.126 A briefing paper on Authentix, Inc. states:

“The immediate introduction of mass serialization at the unit level is an enabler that will lead to better control and management of the supply chain. Many of the benefits predicted from RFID technology can initially be accomplished using barcode technology. Additionally, establishing a data management infrastructure around barcode technology now will simplify RFID implementation later as that technology matures. Authentix has invested in the development of customized product tracking and anti-diversion software and web enabled data management and reporting systems.”

3.127 The addition of covert, overt, and forensic markers can be done for the cost of cents or tenth of cents per unit.

Protexxion by Bayer Technology Services

3.128 This technology provides authentication of products based on natural surface properties to protect from counterfeiting. It uses laser surface authentication connected to a database that can tell if the scan is a valid entry (match) for a specific product. This test is virtually impossible to fake and requires no modification of the object working on many different surfaces and allows products to be traced. The signature data is less than 1Kb (possibly 100 Bytes) and so can be stored centrally.

3.129 Flat scanners can be included in production lines, and can deal with products in a line at a maximum speed of 4m per second. These scanners record the signature of the products as they are produced and record it in a database. Field scanners are also available for

verification that are smaller and can be moved. It takes a few seconds to recognise a scan out of millions based on scanning an area 2cm by 3cm, and has a reliability of 1 error out of 10²⁰. It is possible to place security seals on products for small scale production.

- 3.130 The costs of operating the scheme include the scanners and payment of a license fee per production scan. The first commercial use is planned in 2008, but there was no indication of cost.

Hyperlabel Technologies, Inc.

- 3.131 A presentation related to Hyperlabel Technologies Inc, entitled “A Unified Approach to Product Serialization, Product Security, and Brand Awareness” was given by Don Korn to the WHO IMPACT study in March 2007.
- 3.132 The author states: “There is a desire to authenticate products in the supply chain, and it would be ideal if the patients could also check products.” Brand awareness in pharmaceuticals markets is diminishing, and there is a lack of customer engagement after purchase. Florida requires authentication of digital signatures from June 2006; this Hyperlabel technology supports NIST (National Institute of Standards and Technology) and standard PKI (Public Key Infrastructure) digital signatures.
- 3.133 Hyperlabel is invisible infrared tags over the entire package or label. These tags include a unique item ID and can be scanned in any orientation. Each tag at each position on the product is unique and can be linked to a database similar to RFID but involving print and not a chip. Hyperlabel is cost effective at the item level where packaging or contents are unsuitable for RFID. It is invisible and partly covert (with zero impact on the packaging design). The database can alert the user if there are multiple matches.
- 3.134 Hyperlabel can be verified by the user if they are given a scanner to enable them to read the Hyperlabels. All the product information can be stored in tags or they can direct readers to the internet for updated information.

Table 5.5: Claimed benefits of Hyperlabel (copied from report)

Characteristic	2D barcode	EPC Gen2 RFID	Hyperlabel
Packaging design impact	Obtrusive	Can be high	Zero
Anti-counterfeiting	No	Limited	Yes
Supports full web interactivity	No	No	Yes
Low cost per item	Yes	No	Yes
Auto scannable	Manual	Automatic	Semi-automatic
Protects privacy	Yes	No	Yes

Note: Many of these technologies are compatible with other technologies or coding such as barcodes and RFID, including the use of FractueCode laser signature on products.

JDSU Anti Counterfeit products

- 3.135 The information regarding JDSU is taken from presentations to an EMEA conference in September 2006.
- 3.136 JDSU SecureShift provides brand and product authentication at a number of different levels. The protection is based on the addition of extra components or features to the packaging or product that are hard to copy/manufacture without authorization. These features are then available on authorized products for authentication of genuine status. Any product without the extra feature/components is easy to recognize as a counterfeit product. JDSU offers overt, covert, and forensic security measures.
- 3.137 The overt include colour shifting inks that should be printed in simple patterns to emphasise the significance of the colour-change. Product authentication is based upon verification of the optical effect and correct colour only. In order to increase accuracy of authentication there is an option to use a verification card. This card has an opening surrounded by the reference colours, to enable authentication by verification of similarity. The human eye is generally extremely sensitive to colour differences.
- 3.138 Covert features include Infra-red and Ultra-violet phosphors and need special light in order for them to be read. There are also forensic markers in the ink that can only be read with a 400x or more optical microscope. In reality drug counterfeiters usually do not even make an attempt to copy the JDSU SecureShift items so the forensic protection is more or less redundant.
- 3.139 Extra security should be built in from the start to prevent the need to flush old packets out of the system when new security measures are introduced. The features are compatible with RFID or track and trace features. In most cases the complete solution with all features implemented add up to an amount in the range of one or two US dollars per thousand units in production/packaging cost.

Alcan Packaging Global Pharmaceutical Packaging

- 3.140 This information relating to Alcan is taken from an EMEA Conference in September 2006.
- 3.141 In order to provide both contingency of supply, as well as regional supply sources, Alcan has developed a network of four dedicated N'CRYPT® manufacturing sites. N'CRYPT® technologies, along with hand-held reading devices in the case of covert features, offer a wide range of authentication choices for market stakeholders. The anti-counterfeit technologies applied by Alcan Packaging fall within four main categories:
- 1 Security print
 - 2 Special inks and coatings
 - 3 Unique optical devices

4 RFID and mass serialization

3.142 An important idea in the selection of anti-counterfeit technologies is combining features to create multi-layered solutions. This tenet has been strongly promoted by the FDA and other governmental organisations. Much like building blocks, N'CRYPT® features have been positioned as complementary parts of a total solution. Many factors influence the cost of implementing an anti-counterfeit feature, including:

- (a) cost of technology selected (material cost, bespoke or transferable, etc.)
- (b) necessity of a reading device
- (c) impact on manufacturing and/or packaging process
- (d) need to educate supply chain stakeholders and consumers and
- (e) efficient management of the distribution chain.

SICPA (CONFIDENTIAL)

Supply Chain Organisations

The Global Healthcare User Group (GS1 HUG™)

3.148 The Global Healthcare User Group (GS1 HUG™) www.gs1.org/hug is a voluntary and open group formed by 40 leading pharmaceutical and medical devices companies, wholesalers, hospitals and trade associations from around the world.

3.149 The GS1 System is the most widely used numbering and data carrier system throughout the world. Over 1 million users across 145 countries and across more than 24 industry sectors have adopted what is today known as the GS1 System. It is recognised by organisations such as the International Standards Organisation (ISO), the American National Standards Institute (ANSI) and the European Committee for Standardisation (CEN).

3.150 Agreement on a global standard for the Data Carriers to be used for different packaging levels down to unit-dose and unit-of-use level (where and when to use which barcode type like EAN-13, GS1-128, RSS, Data Matrix or RFID tags) and establishing specifications for printing/scanning/quality is an important next step. Linear barcodes such as code 128 have also been used.

3.151 The data structure for the serial number, the Electronic Product Code (EPC) has been developed to be completely compatible with existing data structures utilized by regulatory agencies and pharmaceutical companies to identify products. It is essentially a Global Trade Item Number (GTIN) appended with a serial number assigned by the manufacturer. The GTIN is completely compatible with the EAN-13 used in some Member States such

as the UK, but is also compatible with local product identification systems such as the Italian AID number and the German PZN.

PGEU (Pharmaceutical Group of the European Union)

3.152 PGEU broadly supports the adoption of track and trace technology. Pharmaceutical companies have been experimenting with a range of new technologies such as radio frequency identification technology (RFID) and optically variable devices (OVDs).

3.153 Overall, PGEU does not identify a specific preference for one particular technology providing the following principles are adhered to:

(a) Technology facilitates the identification and reporting of suspect medicines at pharmacy level, and that fully integrated reporting mechanisms are in place to ensure quick and effective action is to be taken once a suspect item is identified.

(b) Technology is user friendly and practical and above all is not an impediment to the efficiency of the pharmacy; and

(c) Technology does not impose disproportionate costs burdens in the pharmacy.

3.154 A number of supply chain innovations (e.g. altering its configuration), have been tried, with the aim improving the security of the supply chain. However, PGEU has viewed these developments with some concern as they potentially pose risks to the level of efficiency and comprehensive supply of medicines that is characteristic of the current system in Europe. PGEU argues that the most appropriate approach would be to focus more on the coordinating activities of supply chain partners rather than reshaping current supply chains.

GIRP 2005

3.155 A position paper by GIRP (The European Association of Pharmaceutical Full-Line Wholesalers) discussed policies to avoid the risk of counterfeit medicines (2005).

3.156 GIRP identified the main targets for counterfeiters as:

(a) High value lifestyle medicines

(b) High value lines

(c) High volume, mid-priced, medicines

3.157 Internet and mail order constitute the highest risk for the entry of counterfeits into the market.

3.158 Anti-counterfeit measures adopted by GIRP members included:

(a) Careful selection of suppliers.

- (b) Systematic sampling of products, especially from new suppliers.
- (c) Special training on good distribution practices.
- (d) Development of a harmonized European track and trace system.

“A uniformed track and trace system for Europe still lacks the affordable, well proofed and effective technology which would allow for the implementation of a seamless track and trace procedure throughout the supply chain without resulting either in sky rocketing costs or, unacceptable delays for pharmacies and patients. The national identification number, expiry date and batch number in machine readable format are prerequisites for any kind of coding system.”

- (e) Immediate alerting to authorities and manufacturers of suspect products.
- (f) Efficient auditing and recall procedures.

GIRP 2007

3.159 This material is from a GIRP conference in September 2007.

3.160 Harmonised medicine codes are a pre-requisite for introducing track and trace.

3.161 Having assessed the impact of all technologies, GIRP and its members want to implement

- (a) – as data structure: GS1 numbering system and
- (b) – as data carrier: 1D or 2D code.

3.162 Data matrix code is preferred, as it allows for further content expansion and it may cover additional needs of manufacturers, whereas RFID is a future technology only.

3.163 GIRP and its Members want to remain as up to date as possible, which involves finding a balance between advancing technologies and practical solutions. It sees problems with RFID techniques:

- (a) Data protection not readily discussed.
- (b) High Frequency (13.56 MHz): accuracy of reading not given: no mature technology, liquids, aluminum and glass will lead to error rates > 30 per cent.
- (c) Ultra High Frequency (2.45 GHz), accuracy of reading is improved, however: no agreed standard in place yet, higher costs of multi-read-tags, possible harm to the molecular structure of medicines.

3.164 GIRP also sees problems with serial numbers.

3.165 GIRP could agree to the non-exclusive use of a serial number, but the exclusive use causes problems such as data required ad-hoc that may be missing e.g. identification, batch number, expiry date, which should come from a database. There are many unsolved questions: Who is in charge of the database? Who owns the data? Who pays for the costs of the database? Who organises the data transfer? Who is guaranteeing the continuous availability and performance within the supply chain?

EFPIA 2005

3.166 EFPIA presented a 'White Paper' on anti-counterfeiting in November 2005. This included the view that anti-counterfeiting efforts would benefit from improvements in the following areas: EU legislation, international collaboration, definition of the roles of the stakeholders involved in the supply chain, control and transparency in the supply of medicines, and communication.

3.167 With regard to the EU legislation, EFPIA endorses the recommendations of the Council of Europe, as found in the Harper report. The legal system should facilitate close cooperation at the national and international level, for example by providing obligatory exchange of information between customs, public health authorities, police, and rights holders.

3.168 The legal environment should also target counterfeiters, with clear crime definition and sanctions commensurate to the level of the crime, and promote quick exchange of information among customs authorities. Communication aimed at raising awareness directed to the broad public should mainly be done by the public authorities. Alliances and partnerships could be done between the industry and healthcare and patients associations.

3.169 With regard to the supply chain control, EFPIA recommends a supra-national approach involving track and trace systems, a licence system for selling medicines on the Internet, a certificate system for wholesalers and safeguards for the supply of packaging materials. The track and trace system should be based on a pan-European barcode standard, with RFID systems seen as a mid to long term solution, due to its current development status.

EFPIA 2006

3.170 In 2006 EFPIA presented another report, on the identification and coding of pharmaceutical products in Europe.

3.171 According to this assessment, experience within the pharmaceutical industry (pilot projects) and other sectors show that the technology of RFID is not mature enough and is not able to meet all expectations of the industry for the time being. According to experts, it may not be fully available for at least another 10 years. Furthermore, the high costs associated with this technology make it difficult for it to be implemented by all stakeholders.

- 3.172 Any technology used with medicines has to be fully reliable and applicable. EFPIA has therefore identified other solutions that could help to improve the coding of medicines, such as:
- (a) EAN 13: Can identify name, company and country
 - (b) EAN 128: Can identify name, company, country and around 10 more parameters. The main problem is that it takes a lot of space in the package
 - (c) 2D (i.e. Data matrix): Can cover multiple information and takes almost no space in the package
- 3.173 Both EAN 128 and 2D respond well to needs identified (although EAN 13 does not allow product serialisation). While 2D is slightly more expensive, it offers significant advantages as it can include more information in a smaller area and provides more flexibility to incorporate future needs.
- 3.174 EFPIA therefore recommends a 2D (2 Dimension Data Matrix) Bar Code system to be introduced across Europe. This mechanism would include the use of unique serialisation numbers for each secondary packaging unit distributed and sold. It would enable the identification and verification across the entire supply chain, therefore improving transparency and patient safety, and helping fight serious problems like counterfeiting.
- 3.175 The new system can be adopted progressively (e.g. first at a batch level, second at a product level) without requiring a radical change of all European coding systems, but leading to a smooth and progressive harmonisation of the technologies used in Europe and worldwide.
- 3.176 The adoption of a 2D system does not prevent the adoption of an RFID system at a latter stage nor does it represent a double cost. Experience has shown that RFID technology is not workable at present but would certainly be a natural progression of the system.
- 3.177 EFPIA wishes to address this issue urgently in order to prevent the continued fragmentation of coding standards across the EU, the fracturing of the supply chain, and in order to realise the patient safety benefits. With respect to lines of action, EFPIA will:
- (a) Engage with current European initiatives to put across a common Industry standard.
 - (b) Promote the recommended system towards relevant EU bodies.
 - (c) work to highlight compliance and patient safety issues associated with lack of adoption of the recommended system.
- 3.178 Belgium uses an EAN 128, France uses an EAN 39, The Netherlands and Portugal are considering EAN schemes while other Member States have a wide variety of numbering regulations and policies are changing.

- 3.179 EFPIA coding costs presentation: (September 2007).
- 3.180 Manufacturer costs: Installation of Printing equipment and line data collection to Product
- 3.181 Serialisation Database ~ €50 -100 m (one off)/ line x 3000 – 6000 lines, or approximately €0.15-0.6 bn. Also need a data interchange network.

EFPIA 2007

- 3.182 EFPIA gave a presentation on coding costs and the harmonisation of product codes in September 2007.
- 3.183 There are widespread concerns within industry that opportunities are being lost since the standardised and unique coding of medicines through a common pan - European authentication and verification system could significantly improve patient safety while enhancing the security and efficiency of the medicines supply chain. Additionally, from a commercial perspective there is a strategic value for industry to support the introduction of a common system across Europe since the increasing number of local systems/solutions has a significant cost for industry. In this respect, it was noted that the environment does not remain still and further local solutions may be imposed.
- 3.184 The EFPIA recommendation for a unique data carrier is the implementation of a data matrix ECC 200 on secondary packaging of all pharmaceutical products sold in Europe.
- 3.185 The main advantage of the GTIN is that it delivers trade item data in a consistent format and structure. It employs the globally accepted and utilized EAN/UCC System whose language is understood by the global marketplace and is managed by GS1, a non profit and neutral organisation which has taken a leading role in establishing a global multi-industry system of identification and communication for products, services and locations based on internationally accepted and business led standards.

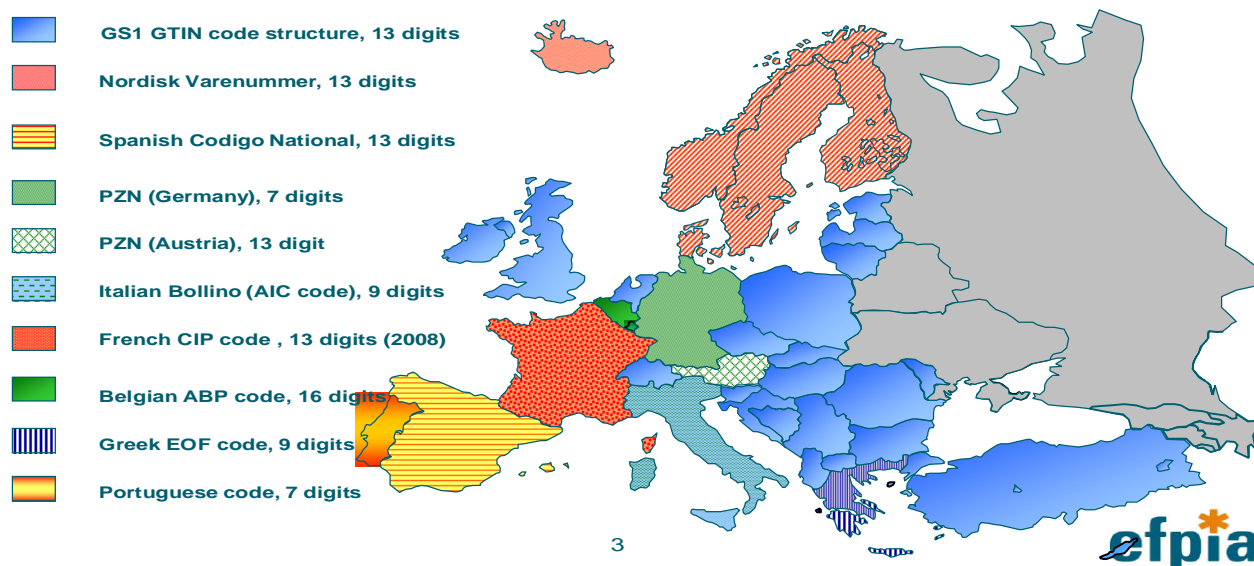
Use both codes (national product code + GTIN)

- 3.186 The 'Data Matrix' ECC200 recommended by EFPIA has the attribute of being able to hold a relatively large amount of information as opposed to the traditional one-dimensional bar code. This would allow manufacturers to encode the recommended GTIN code in addition to the existing national product code. The data carrier could therefore hold two product identification codes.
- 3.187 The option of encoding both product codes could enable a transitional period until the time to phase out the existing national product code becomes appropriate. The downside is that this is likely to increase the size of the 2D bar code symbol. It may also generate complexities as well as confusion.

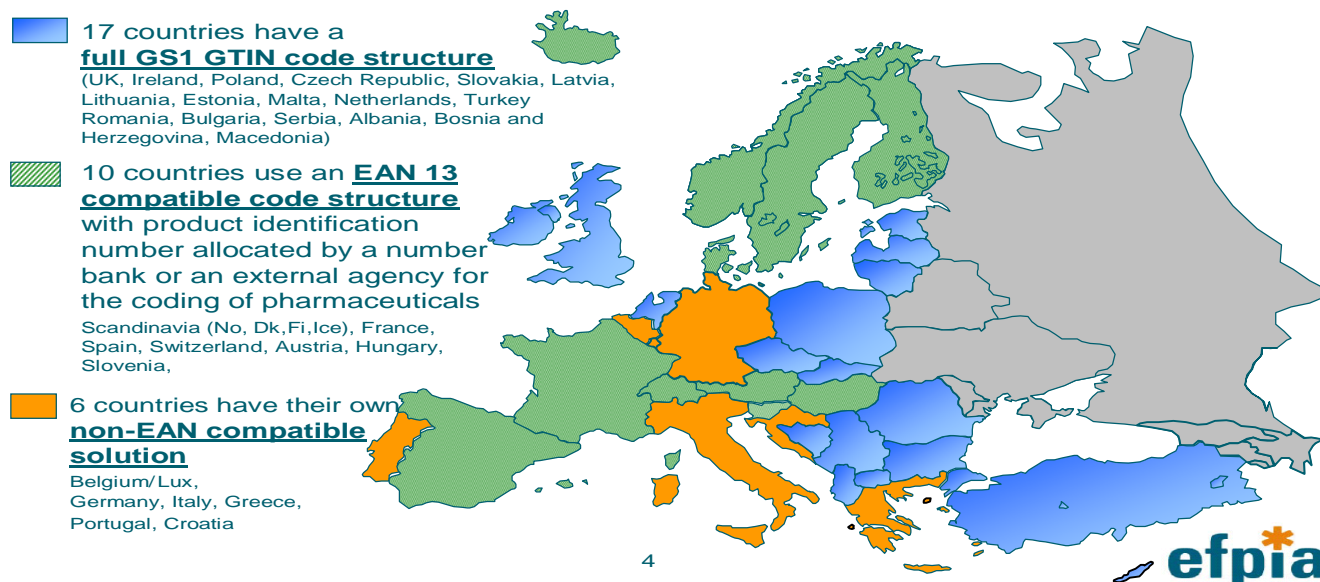
Pseudo GTIN

- 3.188 Another option would aim to retain the existing national codification systems and integrate them in a GS1-128 syntax, which is the global EFPIA recommendation allowing readability of identification codes in an harmonized way (GS1 to allocate – where appropriate - specific prefix numbers for the pharmaceutical industry in those countries (e.g. Germany) with national codification systems (use of ‘pseudo GTIN’)) as is the case for France.
- 3.189 France is the first country in Europe to have a legal framework with a precise calendar for implementation of a data matrix ECC200 on each medicine secondary packaging containing: product code (pseudo GTIN), batch number and expiry date. Other Member States who do not wish to adopt a pure GTIN could follow this example. It must be noted that this option has a number of disadvantages. Without a clear code, the manufacturer can only be identified indirectly, which causes a slight delay in the response time with the link to the database.
- 3.190 National codes will still exist for some time, but it will be necessary to bridge a gap between national codes and a harmonized codification vision based on the GTIN.

Identification across Europe : Overview
National Codification Systems (I)



Identification across Europe : Overview National Codification Systems (II)



3.191 France has adopted 2D Data Matrix as of 1 January 2008 (first in Europe), but it is also being adopted in Spain, the Netherlands and Turkey. Turkey and Spain are passing new legislation mandating the use of a serial number in 2008.

EFPIA January 2008.

3.192 EFPIA presented another paper in January 2008 (“A vision for the coding and identification of pharmaceutical products in Europe”)

3.193 EFPIA would like a central database system operated by an independent (not for profit) organisation that would be owned by industry stakeholders. Manufacturers would place the serialisation code on the packet (prescription item) and this would be checked against the database when it was dispensed. European co-ordination is needed to prevent further fragmentation of the European market with different coding and tracing requirements in different Member States.

3.194 The product serialisation would be arranged in a code as follows:

- (a) The product code, referred to as a **GTIN**, uses the AI of 01 and is a fixed field length of 14 numeric digits.
- (b) The serial number uses the AI of 21 and is a fixed field (in the EFPIA recommendation) of 20 numeric digits non-zero leading (i.e. the first digit cannot be a zero). This must contain a random or non-predictable element.
- (c) The expiry date uses the AI of 17 and is a fixed field of 6 numeric digits in the predefined format of YYMMDD (Year=YY, Month=MM and Day=DD).

- (d) The batch code uses the AI of 10 and is a variable length field, up to ten alphanumeric digits in length and is always placed at the end of the code structure.

Costs

3.195 Installation cost of data matrix “printing” and reading equipments plus line data collection plus product serialization database (costs for Industry)

- (a) €50,000 –100,000 per line for 3,000 – 6,000 lines

- (b) Altogether ~ €150 - 600 million

- (c) Installation cost of 2D data matrix readers and software upgrade (costs for pharmacies)

- (d) €1500 per pharmacy (€300 - 400 per reader)

- (e) €2,000,000 (assuming 30,000 installations)

3.196 Cost of running/using data interchange network for verification of serial number at the dispensing point (and database update).

3.197 ~ €0.01- 0.02 per pack (preliminary estimate)

3.198 It must be noted that comparatively speaking, it will be significantly less costly than systems involving expensive new technologies such as RFID, and, being based on proven technology, significantly more reliable. Also, this standardized system can be expected to be significantly lower in cost both in terms of implementation and operation, and higher in efficiency and effectiveness compared to implementing several different systems at European level. In any case the costs of inaction will far exceed the cost of implementation of the system in medium and long term.

3.199 Administrative costs of reimbursement systems should be significantly reduced in the long term. The system will not have immediate effects on wholesalers (but may help recall procedures) and can lead to a more continuous tracking system later.

Planned pilot study

3.200 The pilot, planned for Q4 2008, will focus on a single European location at a regional level. Current assumptions for the pilot are:

- (a) A maximum pilot size of 200 pharmacy outlets.

- (b) Allowance for up to 1 million line item packs to be individually coded.

- (c) A single, hosted server system to provide most of the functionality required for the main pilot and its full implementation.

- 3.201 The system will demonstrate the capability to operate using specified performance criteria. EFPIA has allocated a budget of €1 million to this project.
- 3.202 System response time should be under 1 second from the time of scanning.
- 3.203 System reliability/robustness currently targeted at greater than 99.9 per cent, in case of system downtime, need store transaction on local system for verification at a later stage.

Problems with RFID tags: (EFPIA)

- 3.204 Some RFID tags are currently not achieving satisfactory read rates. Despite many promising applications, tags are still not 100 per cent reliable with anything from 3-5 per cent error rates.¹⁵ According to experts, it may not be fully available for at least another 10 years.
- 3.205 Costs remain high; current passive tag cost estimates range from \$0.15 to \$0.75 (€0.10 - 0.51), with the volume of tags purchased having a significant impact on the cost.
- 3.206 According to the European Commission communication on RFID, there is a need for clear and predictable legal and policy framework to make this new technology acceptable to users. This framework should address: ethical implications, the need to protect privacy and security; governance of the RFID identity databases; availability of radio spectrum; the establishment of harmonised international standards; and concerns over the health and environmental implications.
- 3.207 The adoption of a 2D system does not prevent the adoption of an RFID system at a latter stage nor does it represent a double cost. Experience has shown that RFID technology is not workable at present but would certainly be a natural progression of the system.
- 3.208 Note: (Europe Economics) 2008 media report said that RFID tags used for airline baggage tags had an error rate of less than 1 percent (bar codes failed in 15 per cent of cases). These tags cost \$0.2 (compared to less than one cent for bar codes). However, airline baggage is a very different use with more physical stress to the tags and shorter time periods or tag lifetimes required. One firm has claimed it can produce tags which last over 10 years but these can cost over \$5.

¹⁵ Michael, K, & McCathie, L, The pros and cons of RFID in supply chain management, Proceedings of the International Conference on Mobile Business, 11-13 July 2005, 623-629. Copyright IEEE 2005.

There are many different and evolving coding schemes in Europe

Table 5.6: Coding Schemes

	Country	National Identification Number*	Digits - Natl' ID Number	Identifies the product presentation uniquely*	Identifies the individual pack uniquely*	Identifies the licence holder*	Code Structure*	Digits of Natl' code	Bar code*	Scope of coverage of the code	Purpose of the codification system	Body in charge of codification	Legal Coding Requirements*	Is the code used for reimbursement purposes?
1	Austria	Pharmazentralnummer (PZN)	7	yes	no	indirectly in the database	Country ID (2) + Sector (4) + PZN (6) + check (1)	13	EAN 13	All proprietary medicinal products	Reimbursement	Austria Association of Pharmacists EAN (barcode authority)	no	yes
2	Belgium	Code National (APB code)	7	yes	yes	indirectly in the database	APB (7) + Sequential number (8) + check digit (1)	16	Code 128 subset c	All reimbursed public extern packs (Belgium market)	Reimbursement	Association Pharmaceutique Belge (APB)	yes	yes
3	Bulgaria	n/a	n/a	yes	no	indirectly in the database	GTIN	14	EAN 13 or EAN 8	All pharmaceutical products	Identification		no	no
4	Croatia	National code number	10	yes	no	indirectly in the database	ATC (generic) code (7) + product (SKU) ID (3)	10	no bar code	All pharmaceutical products	Reimbursement	Croatian Ministry of Health Croatian Institute for Health Insur.	no	yes
5	Cyprus	no	n/a	yes	no	yes	EAN Structure/GTIN	13	EAN 13 or EAN 8	All pharmaceutical products	export purposes	GS1 Cyprus (?)	no	no
6	Czech Rep	no	n/a	yes	no	yes	EAN Structure/GTIN	13	EAN 13	All pharmaceutical products	Identification	State Institute for Drug Control	yes	no
7	Denmark	Nordisk Varenummer	6	yes	no	indirectly in the database	704626 + NMD (6) + Check Digit (1).	13	EAN 13	All proprietary medicinal products	Identification	Nordic article number office (Norsk Medisinaldepot (NMD) DLI - Dansk Lægemeddel Information	yes	no

Appendix 2: Track and Trace Technology

	Country	National Identification Number*	Digits - Nat'l ID Number	Identifies the product presentation uniquely*	Identifies the individual pack uniquely*	Identifies the licence holder*	Code Structure*	Digits of Nat'l code	Bar code*	Scope of coverage of the code	Purpose of the codification system	Body in charge of codification	Legal Coding Requirements*	Is the code used for reimbursement purposes ¹
8	Estonia	no	n/a	yes	no	yes	EAN Structure/GTIN	13	EAN 13 or EAN 8	All pharmaceutical products			no	no
9	Finland	Nordisk Varenummer	6	yes	no	indirectly in the database	704626 + NMD (6) + Check Digit (1).	13	EAN 13	All proprietary medicinal products	Identification	Nordic article number office (Norsk Medisinaldepot (NMD) Lääketietokeskus Oy	yes	no
10	France (till end 2010)	AMM code (also called CIP code 7 digits)	7	yes	no	indirectly in the database	CIP code (7)	7	Code 39		Identification	Club Inter Pharmaceutique (CIP) AFSSAPS (French Health Products Safety Agency)	yes	yes
	France (2011)	AMM code (also called CIP 13)	13	yes	no	indirectly in the database	Prefix 3400 + "AMM" (Market authorisation) + check digit (1) / AMM will be considered on 13 digits from 2009	13	2D Data Matrix	All pharmaceutical product	Reimbursement, Traceability	Club Inter Pharmaceutique (CIP) AFSSAPS (the French Health Products Safety Agency)	yes	yes
11	Germany	Pharmazentralnummer (PZN)	7	yes	no	indirectly in the database	PZN (6) + check digit (1)	8	Code 39	All reimbursed medicines	Reimbursement	Informationsstelle für Arzneispezialitäten GmbH (IfA)	yes	yes
12	Greece	Unique Product Code (assigned by EOF)	9	yes	yes	indirectly in the database	EAN number for medicinal products (3) + EOF product code (9) + Check digit (1)	13	UCC/EAN-128	All pharmaceutical products	Reimbursement, Statistics	EOF (National Organization for Medicines) ELKESIP, EAN/UCC barcode authority	yes	yes

Appendix 2: Track and Trace Technology

	Country	National Identification Number*	Digits - Nat'l ID Number	Identifies the product presentation uniquely*	Identifies the individual pack uniquely*	Identifies the licence holder*	Code Structure*	Digits of Nat'l code	Bar code*	Scope of coverage of the code	Purpose of the codification system	Body in charge of codification	Legal Coding Requirements*	Is the code used for reimbursement purposes ¹
13	Hungary	no	n/a	yes	no	yes	EAN Structure/GTIN	13	EAN 13	All pharmaceutical and therapeutical equipments	Reimbursement, Identification	Hungarian Ministry of Health	no	yes
14	Ireland	IPU code	5	yes	no	yes	EAN Structure: Country ID:539 (3) + Manufacturer (4) + product ID (5) + check (1)	13	EAN 13 or EAN 8	All products sold in pharmacies	Identification	ANAI Article number association of Ireland Irish pharmaceutical Union (IPU)	yes	no
15	Italy	AIC code	9	yes	yes	indirectly in the database	AIC code (9 characters)	9	Code 39/ code interleave 2/5	All reimbursed medicines	Reimbursement	Italian Ministry of Health	yes	yes
16	Latvia	no	n/a	no	yes	yes	EAN Structure/GTIN	13	EAN 13	All products sold in Pharmacies	Identification	GS1 Latvia	no	no
17	Lithuania													no
18	Malta	no	n/a	yes	no	yes	EAN Structure/GTIN	13/8	EAN 13 - EAN 8		Identification	EAN Malta CSSD (the Central Sterilization Department of the Maltese public hospital)	no	no
19	Netherlands	KNMP product code	7	yes	no	indirectly in the database	KNMP (7) + check digit (1)		Code 39	All (registered) medicines, OTC, medical devices.	Reimbursement & Identification	Royal Dutch Association of Pharmacists (KNMP)	no	yes
	Netherlands	EHIBCC code		yes	no	indirectly in the database	labeler + trade product number + identification unit of measure + check digit	14	Code 39	Medicines and medical devices	Identification	Royal Dutch Association of Pharmacists (KNMP)	no	no

Appendix 2: Track and Trace Technology

	Country	National Identification Number*	Digits - Nat'l ID Number	Identifies the product presentation uniquely*	Identifies the individual pack uniquely*	Identifies the licence holder*	Code Structure*	Digits of Nat'l code	Bar code*	Scope of coverage of the code	Purpose of the codification system	Body in charge of codification	Legal Coding Requirements*	Is the code used for reimbursement purposes ¹
	Netherlands	EAN code		yes	no	yes	country + manufacturer + number + checkdigit	13	EAN 13	Medicines, OTC, medical devices	Identification	GS1 Netherlands	no	no
20	Norway	Nordisk Varenummer		yes	no	indirectly in the database	704626 + NMD (6) + Check Digit (1).	13	EAN 13	All proprietary medicinal products	Identification	Nordic article number office (Norsk Medisinaldepot (NMD))	yes	no
21	Poland	Registration number (MoH)	4	yes	no	indirectly in the database	590: Country Prefix (3) + Authorities Prefix (4) + Reg Number (4) + Pack ID (1) + check (1)	13	EAN 13	All pharmaceutical products	Identification	Polish Ministry of Health	yes	no
22	Portugal	Registration Number of Medicine Presentation	7	yes	no	no	start character + sequential number (6) + check digit (1) + end character	9	Code 39	All medicines sold through pharmacies	Reimbursement	INFARMED	yes	yes
23	Roumania	n/a	n/a	yes	no	yes	594: Country Prefix (3) + 47MM Manufacturer ID (4)+ Product ID (5) + Check digit (1)	13	EAN 13, EAN 8 and ITF-14	85% of Romanian pharmaceutical products	Identification	EAN Romania	no	no
24	Slovakia	no	n/a	yes	no	yes	EAN Structure/GTIN	13	EAN 13	Approximately 10% pharmacies use EAN coding system	Identification		no	no
25	Slovenia	no	n/a	yes	no	indirectly in the database	383:Country Prefix (3) + 700X Authorities	13	EAN 13	All pharmaceutical products	Identification		yes	no

Appendix 2: Track and Trace Technology

	Country	National Identification Number*	Digits - Nat'l ID Number	Identifies the product presentation uniquely*	Identifies the individual pack uniquely*	Identifies the licence holder*	Code Structure*	Digits of Nat'l code	Bar code*	Scope of coverage of the code	Purpose of the codification system	Body in charge of codification	Legal Coding Requirements*	Is the code used for reimbursement purposes ¹
							Prefix (4) + Reg N. (5) + check (1)							
26	Spain	"Código nacional" CN	6	yes	no	indirectly in the database	84 7000 + CN(6) + Check digit (1)	13	EAN 13	All authorised medicinal products	Reimbursement, Traceability	SANIDAD - Spanish Ministry of Health	yes	yes
27	Sweden	Nordisk Varenummer	6	yes	no	indirectly in the database	704626 + NMD (6) + Check Digit (1)	13	EAN 13	All authorised medicinal products	Identification	Nordic article number office (Norsk Medisinaldepot (NMD))	yes	no
28	Switzerland	Swissmedic number	8	yes	no	indirectly in the database	EAN Structure: Country ID (2) + Sector (2) + Product ID (5) + packing code (3) + check (1)	13	EAN 13	Proprietary Medicinal products	Identification	Swiss Foundation REFDATA Swissmedic (Swiss registration authority)	no (except narcotics)	no
29	UK	no	n/a	yes	no	yes	Country ID (2) + Manufacturer (5) + product ID (5) + check (1)	13	EAN 13	All products sold in Pharmacies	Identification	ANA Article number association (EAN Member org)	no	no
30	Serbia & Montenegro	no	n/a	yes	no	yes	EAN Structure/GTIN	13	EAN 13, EAN 8	All pharmaceutical products	Identification	GS1 Serbia & Montenegro	yes	no

Source: EFPIA "Overview of codification systems in Europe 2008."

Table 5.7: Key stakeholder benefits

Objectives	Industry	Governments/ Purchasers	Pharmacists	Wholesalers	Patients
Improve product security	Reduce risk of counterfeits entry into the legitimate supply chain Facilitate effective product recalls	Address the growing risks of counterfeits entering the legitimate supply chain Improve effectiveness of product recall procedures (pharmacovigilance)	Reduce pharmacists' liability risk for delivering counterfeits or corrupted products Prevent dispensing errors Facilitate product recall procedures	Reduce wholesalers liability risk for delivering counterfeits or corrupted products Facilitate product recall procedures	Reassure patients on the quality of medicines they are dispensed
Improve patient safety	Prevent dispensing and dosing errors Ensure the quality of the medicine being dispensed	Prevent dispensing and dosing errors (and avoid associated costs)	Improve patient services provided by pharmacists	Provide wholesalers with the possibility to verify expiry date, batch n° and national identification n° (if applicable)	
Harmonise standards for product coding systems	Avoid incremental production costs for manufacturing and logistics due to 27 different coding systems Ensure the ability to trace back a medicine's origin throughout Europe (inefficiency of national systems to protect the EU market against counterfeits due to the free movement of goods) Reduce the complexity and differentiation across the European market	Ensure interoperability of national coding systems (necessary condition to effectively tackle counterfeits in the EU) Address market access hurdles linked to specific coding systems (clear legal basis for developing pan-European guidelines on identification and authenticity of medicines)	Standardises pharmacy equipment across Europe	Ensure interoperability of national coding systems (efficient logistical supply chain)	
Increase traceability in the supply chain	Allow control and monitoring of the medicine's origin Provide access to improved data sources on sales (possibly real time)	Prevent reimbursement fraud Support administrative handling of reimbursement procedures	Support administrative handling of reimbursement procedures Speeds up payment mechanism	Enable the development of a full track & trace system in the long term	

Source: EFPIA coding solutions – Business case v4.