GIRP RESPONSE TO THE PUBLIC CONSULTATION IN PREPARATION OF A LEGAL PROPOSAL TO COMBAT COUNTERFEIT MEDICINES FOR HUMAN USE - KEY IDEAS FOR BETTER PROTECTION OF PATIENTS AGAINST THE RISK OF COUNTERFEIT MEDICINES

1. INTRODUCTION

GIRP – "Groupement International de la Répartition Pharmaceutique Européenne" – is the European umbrella organisation of pharmaceutical full-line wholesalers. It represents the national associations of over 600 pharmaceutical full-line wholesalers serving 31 European countries, including the major pan-European pharmaceutical wholesaling companies. Employing 140,000 people across a complex web of facilities they distribute 100 billion euros worth of medicines every year. In the performance of their public service role they absolutely guarantee the highest levels of quality, integrity and excellence. GIRP members are the trusted supply chain partners of manufacturers, pharmacists, healthcare professionals and, above all, patients for ensuring medicines safety. They are a vital link between the trusted partners and should this vital link break, the safe and continuous supply of medicines cannot be guaranteed.[1]

GIRP welcomes the European Commission's public consultation on key ideas for better protection of patients against the risk of counterfeit medicines. The public consultation comes at the right time, following the extensive debate on how to address the increasing threat to public health and safety from counterfeit medicines penetrating the market and reaching patients.

2. COUNTERFEITING OF MEDICINAL PRODUCTS – AN INCREASING THREAT TO PUBLIC HEALTH AND SAFETY

GIRP underlines its commitment to the fight against counterfeit medicines and strives to exclude any risk of counterfeit medicines entering the legal supply chain to ensure that the patient receives the genuine product at points of dispensing. The members of GIRP are committed to a zero tolerance approach to the risk of counterfeit medicines in the trusted legitimate supply chain and stress the need to fully cooperate with all supply chain partners and activities. In order to maximise impact, an efficient anti-counterfeiting strategy requires a co-ordinated, long-term stakeholder effort, where all share

[1] For further information please see the GIRP Position Paper on "The Role of Pharmaceutical Full-line wholesalers" under www.girp.org.

accountability, all bear responsibility and all invest resources. The fight against counterfeit medicines can only be successful if carried out together in a joint approach.[2]

GIRP is very supportive and actively involved in the wide range of anti-counterfeiting initiatives currently ongoing at the European and international level. The work of the association in the field extends to but is not limited to its collaboration with the World Health Organisation's (WHO) International Medicinal Product Anti-Counterfeiting Task Force (IMPACT), the Council of Europe as part of the Council of Europe/ Directorate for the Quality of Medicines and HealthCare (EDQM)/DBO: Committee of Experts on minimising public health risks posed by counterfeiting of medical products and related crimes (CD-P-PH/CMED), and through the 'Safe Supply' chain initiative with GIRP's supply chain partners, the manufacturers and pharmacists. -

GIRP highly appreciates the risk assessment based approach the European Commission has taken in the consultation document.

2.1 Risk assessment

GIRP concurs with the European Commissions' observations on worrying trends on counterfeit medicines. Each year there is an increase in the number of counterfeit medicines seized. Previously counterfeiters mostly targeted so called 'lifestyle' medicines, whereas there currently an increasing trend towards the targeting of life saving medicines.

While it is true that counterfeiters increasingly target the legal supply chain, the number of instances of counterfeit medicines penetrating the legitimate supply chain remains low by comparison to the number of counterfeit medicines reaching patients through unregulated and illegal distribution channels. Moreover, the situation in Europe is different to other regions of the world. Europe is privileged to already having high standards in the pharmaceutical supply chain and through regulatory procedures. Thus, the number of cases of counterfeit medicines is limited in scope. Nevertheless, as highlighted beforehand, pharmaceutical full-line wholesalers are very concerned about the risks of counterfeit medicines entering the trusted, legal supply chain and as counterfeits endanger the health of patients, GIRP's members are committed to a zero tolerance approach.

GIRP has identified correlations between the European Union Member States' risk profiles in respect of the probability of counterfeit medicines entering the legal supply chain concerning the organisation of the pharmaceutical market and the supply chain specifically. Bearing in mind that the risk for medicines' categories to be counterfeited are changing, when analysing the EU markets, one can distinguish between product categories and distribution systems with relatively high or low risk profiles. It is therefore crucial to focus measures on product categories and distribution systems with relatively high risk profiles. The measures implemented to combat counterfeit medicines should be

[2] For further information please refer to the GIRP Position Paper on "Avoiding the risk of counterfeit medicines entering the market" under www.girp.org.

based on a sound risk assessment and on an impact assessment of measures proposed and the impact of these measures should be proportional to the costs involved.

Product categories:

In respect to products, it is evident that high value medicines are more likely to be counterfeited. We have observed a significant extension in the product categories which are likely to be counterfeited which range from mostly lifestyle medicines to vital life saving medicines including products which protect against heart diseases, cancer and viral infections, which are profitable enough to be an incentive to counterfeiters. However, to our knowledge, Over the Counter (OTC) and generic medicines have not yet been counterfeited in EU Member States due to the fact that they offer lower financial incentives to counterfeiters.

Distribution systems:

In respect of distribution systems a low potential risk profile seems to correlate with:

- the granting of limited number of wholesaling licenses resulting in clearly identified operators,
- the distribution of medicines only through full-line wholesalers,
- the strict and regular control of distribution licenses,
- the existence of a strongly interlinked supply chain between manufacturers, full-line wholesalers and pharmacies (including legitimate mail order pharmacies)[3] and
- an absence of illegitimate and unregulated internet sales of medicinal products from non-certified sources.

3. THE CURRENT LEGAL ENVIRONMENT REGULATING PHARMACEUTICAL WHOLESALE DISTRBUTION

In the European Union the activity of pharmaceutical wholesaling is regulated through Directive 2001/83/EC, the Community code relating to medicinal products for human use, as amended by Directive 2004/27/EC, Chapter VII "Wholesale distribution", and the Guidelines on Good Distribution Practice (GDP) 94/C 63/03. These provisions offer guidance to pharmaceutical wholesalers in carrying out their activity, laying down that all medicines distributed in a Member State must be covered by a marketing authorization and that medicines can only be bought from and sold to authorised sources. The strict

[3] Illegitimate internet pharmacies are not subject to any kind of regulation or control and have no link to a registered pharmacy. Therefore, they have to be distinguished from legitimate mail-order pharmacies which are registered pharmacies with an online presence and are carried out in accordance with member state rules. Both, 'brick-and-mortar' pharmacies as well as mail-order pharmacies are part of the legitimate pharmaceutical supply chain.

adherence to the following provisions ensures the quality and the integrity of the medicinal product throughout the distribution channel.

Directive 2004/27/EC:

- *Article 76: "Member States shall ensure that only medicinal products for which a marketing authorisation has been granted in accordance with Community law are distributed on their territory."*
- *Article 80 (b): "Holders of a distribution authorisation must obtain their supplies of medicinal products only from persons who are themselves in possession of the distribution authorisation or who are exempted from obtaining such authorisation under Article 77 (3)."*
- *Article 80 (c): "Holders of a distribution authorisation must supply medicinal products only to persons who are themselves in possession of a distribution authorisation or who are authorised or entitled to supply medicinal products to the public in the Member State concerned."*

Furthermore, the Guidelines on Good Distribution Practice (GDP) 94/C 63/03 include provisions on actions to be taken in case of counterfeit medicines being detected in the pharmaceutical supply chain.

However, current legal provisions only cover persons or entities involved in the physically possession and movement of pharmaceutical products and not those otherwise involved.

4. GIRP'S VIEWS ON THE KEY IDEAS FOR BETTER PROTECTION OF PATIENTS AGAINST COUNTERFEIT MEDICINES

GIRP fully agrees that only a "concert of various measures designed to change and improve the current regulatory framework can help to minimise the risk of counterfeit medicines entering the legal supply chain". In this respect, GIRP has for a long time called for a wide range of measures to ensure that only genuine high quality products reach the patients such as clearly defining the responsibilities and liabilities for all actors involved in the distribution chain (including operators involved in the supply chain which are not engaged in the handling of pharmaceutical product such as B2B platforms, brokers, traders and agents); stricter rules and controls of all supply chain operators involved, and applying strict penalties for production, trafficking, dealing, supplying or other related activity that may result in a counterfeit medicines reaching the hands of patients.

GIRP agrees with the European Commission's identification of the three areas of regulation of medicinal products where improvements to the regulatory framework can make a real contribution to protecting the patients in Europe against counterfeit medicinal products. Considering the ambit of activity of pharmaceutical full-line wholesalers, this response will limit itself to those areas which are related to GIRP's members' operations. Therefore, GIRP will limit its reply to addressing issues concerning the distribution of medicinal products already available on the market (i.e. traceability, product integrity, and the legal

framework for the distribution chain as outlined in point 4.1 of the European Commission's consultation document).

4.1. Subject all actors of the distribution chain to pharmaceutical legislation

Key ideas for changes to the EC legislation submitted for public consultation

Clarify that the obligations for wholesalers apply to all parties in the distribution chain, except for those directly distributing or administering to the patient. Brokers, traders and agents would be considered as wholesalers, with the respective obligations stemming from the pharmaceutical legislation.

4.1.1. Background

In most EU Member States, a high numbers of distribution licenses have been granted by the authorities (sometimes by regional but mainly by national authorities) to the various operators active in the pharmaceutical field. In most countries, no differentiation of any kind between the distribution activities and therefore there is no specific license granted for the activity of pharmaceutical full-line wholesaling.

The following list provides an overview (of countries for which the information is currently available to us) of the overall numbers of distribution licenses, which have been granted in comparison to the number of pharmaceutical full-line wholesalers active in these European countries[4]:

- In Belgium the number of wholesaling licenses (grossiste-répartiteur) is 38, however only 11 pharmaceutical full-line wholesalers operate in the country.
- In Denmark between 300 and 350 companies are holders of official wholesaling licenses. In addition, another 150 companies have a license to import and distribute pharmaceuticals from countries outside the EU/EEA area. However only 3 pharmaceutical full-line wholesalers operate, in Denmark.
- In France there are 25 licenses given out by AFSSAPS, out of which 9 are full-line wholesalers (without the wholesalers operating overseas). Further, detailed information on the various types of licenses granted in France can be consulted on the internet under http://afssaps-prd.afssaps.fr/php/etapharm/scr_res.php.
- Germany has granted more than 4,000 distribution licenses, whereas only 15 pharmaceutical full-line wholesalers operate on the national market.

[4] Source: GIRP members (2008).

- In Hungary, 89 wholesale licences have been issued by the Hungarian Institute of Pharmaceuticals (OGYI), whereas only 4 pharmaceutical full-line wholesalers operate in the country.
- In Italy the association of full-line wholesalers, ADF, has 78 members. However, around 494 licenses have been granted. In addition, 230 pre-wholesaling licenses have been granted (pre-wholesalers usually operate under the responsibility for the manufacturer, according to GMP). The licenses' applications are granted in some cases by regional and in other cases by national authorities.
- In the Netherlands 332 wholesale licenses have been issued by the Dutch authorities. In order to be able to distribute branded (Rx) products, the entity needs to have an additional license. Around 300 license holders have both licenses. In addition, 92 'import licenses' and 50 'industry licenses' have been granted, whereas only 3 pharmaceutical full-line wholesalers operate in the Netherlands.
- The wholesale distribution of medicines in Portugal is authorised and regulated by the National Institute of Pharmacy and Medicine (INFARMED). INFARMED has issued 195 official wholesaling licenses for pharmaceutical products for human use, however only 8 pharmaceutical full-line wholesalers are active on the Portuguese market.
- In Spain 45 pharmaceutical full-line wholesalers are operating through around 155 warehouses (each warehouse has its own license) in addition another 150 pharmaceutical full-line wholesaling licenses have been issued. Licenses are granted by the regional authorities.
- In the UK around 1,700 wholesalers' dealers' licenses have been issued, however only 11 pharmaceutical full-lines wholesalers are active on the UK market.[5]

4.1.2. Classification of the supply chain operators and their responsibilities

The distribution of medicines involves in many cases – in addition to pharmaceutical full-line wholesalers –a range of other operators, such as short-line wholesalers, logistic service providers (LSP's) all of which take part in the actual physical handling and movement of medicines. Other operators may include brokers, traders and B2B platforms, i.e. persons and entities that do not actually have any physical contact with the products but merely act as intermediaries.

The current European legislation does not provide for any clear definitions or classifications between the operators of the distribution chain. No distinction is made between the operators and, as a result there are a wide and diverse range of different operators active in the pharmaceutical sector, many of which operate away from the focus of any scrutiny of the authorities (and in some case even knowledge). This is particularly

[5] Source: GIRP members: 2007 (updated 2008)

the case for actors known as brokers, B2B platforms and agents, which currently do not fall within scope any provisions of the EU pharmaceutical legislation.

GIRP agrees that stringent obligations (as currently the case for wholesalers) should apply to all operators in the distribution chain. The consultation document proposes that operators such as brokers, traders and agents would be considered as wholesalers, with their respective obligations stemming from the pharmaceutical legislation. It would be difficult to regard as wholesalers those operators not actually having any physical contact with the medicines and merely acting as intermediaries. For this reason GIRP would propose the establishment of a classification system for the various types of operators active in the pharmaceutical supply chain and more specifically the distribution chain.

GIRP believes that this gap should be acknowledged and measures taken to reconcile this lack of regulation at European level. The classification of the various operators of the distribution chain would facilitate the establishment of responsibilities and liabilities for all involved. GIRP proposes the creation of a classification system in which all involved operators in the distribution chain would be regulated. The classification categories would then be licensed according to the activities involved and levels of responsibilities should be attached through issuing specific licenses, regulated through a European framework.

GIRP would foresee the following classification:

a. Wholesaling operators of the distribution chain

A wholesaling operator (i.e. full-line wholesalers) of the distribution chain includes those which are engaged in the purchase and sale; warehousing; storage; order preparation, and delivery of medicines. They carry and distribute the assortment of products (in range and depth) to meet the needs of those with whom they have normal business relations and deliver all medicines used in their geographical area of activity within a short time limit.

b. Non wholesaling operators of the distribution chain

A non wholesaling operator (i.e. logistics providers) of the distribution chain includes those which are engaged in providing logistic services for part or all of the supply chain management functions for other entities such as manufacturers or suppliers. Third party logistics providers are typically specialized in integrated warehousing and transportation services that can be customized according to the demands and delivery requirements of their customers. They do not hold proprietary rights over the medicines they store or distribute, which makes them distinct from wholesaling operators of the distribution chain.

c. Other operators

Other operators (brokers, B2B platforms, traders) include those not falling under the classification or definition of wholesaling operators and non wholesaling operators of the distribution chain. They are concerned with providing platforms for trade, such as Internet and other communication services. They do not store or distribute the medicines they are

trading, which makes them distinct from wholesaling operators and non wholesaling operators of the distribution chain.

4.1.3 Licensing and responsibilities

All operators involved in the handling and trade of the pharmaceutical products should be subject to stringent regulations, which attract corresponding levels of enforcement. The level of responsibility and liability for all operators within each classification should be identical for one another.

With respect to other operators which are not involved in the actual physical handling of pharmaceutical products, specific stringent requirements dedicated to this activity should be established with equal levels of liability for all actors with their respective obligations stemming from a specific addendum to the pharmaceutical legislation and be enforced through an appropriate licensing system with equally stringent controls.

a. Licenses for wholesaling operators of the distribution chain

All wholesaling operators of the distribution chain (i.e. full-line wholesalers) are currently licensed according to the licensing systems of the Member States in which they are established. Wholesaling operators must meet established regulations which set forth strict minimum requirements for pharmaceutical product storage and security, as well as for the treatment of returned, damaged, recalled and outdated products.

The streamlined establishment of common licensing requirements and renewal schedules should be developed. An efficient mean to gain control in some countries over the enormous number of licenses, would be the introduction of a “sunset clause”, whereby licences, once having been obtained and not used for more than a defined period of time should become automatically invalid. The invalidation of the license should be published.

Certified compliance to GDP has to be guaranteed as minimum requirement for issuing any kind of license in all EU Member States to cover activities involving the handling and distribution of medicines.

With respect to the qualification of the qualified person, the current European legislation does not further specify (Art. 79 (b) of Directive 2001/83/EC) the requirements for the qualification of the qualified person to be designated by the wholesaler. However, those involved in the handling of pharmaceutical products either through the manufacturers’ own distribution, wholesaling, logistic service provision or other should ensure the same level of qualification within a Member State.

Member States have laid down country specific rules for the requirements for the qualification of the qualified person to be designated by the wholesaler.[6] GIRP proposes

[6] Please find in *Annex 1* an overview the qualification of the qualified persons throughout the EU Member States currently designated by pharmaceutical full-line wholesalers.

that the requirement for the qualification of the qualified person to be designated by the wholesaler should be a person with a qualification/degree approved by the respective health authority in the EU Member States or a pharmacist.

An important fact to consider in the reflection of the need to clarify that the responsibilities for wholesale operators of the distribution chain (i.e. full-line wholesalers) is the extreme complexity and the challenges in the distribution sector. While it is clear from the above that many different parties can operate within the distribution chain, this is due to the fact that different and diverse distribution systems are currently established. In addition to pharmaceutical full-line wholesaling, other means of distributing medicines in the national markets include arrangements such as direct distribution, Direct-to-Pharmacy (DTP) distribution, agency distribution etc.

In this respect, it is important to highlight the key role and public service function that full-line wholesalers perform throughout the EU. In most EU Member States, the system of medicines' distribution is based on a public service function, which in several countries is directly placed by law on wholesalers, in others by law on pharmacies (which in turn rely on wholesalers to deliver all medicinal products through a very high service level), in order to guarantee that patients can rely on the continuous and safe supply of all medicines, be it a high priced innovative product, a low priced generic medicine or a seldom used medicine. In this way, even the most isolated patients receive all seldom used, but nevertheless vital medicines – wherever and whenever needed.

Typically, the public service obligation placed on full-line wholesalers contains the following elements. The wholesaler must:

- commit to deliver to any pharmacy over the declared geographic area,
- carry the full range of medicines used in its geographic area of activity;
- carry a stock of medicines guaranteeing usual customers a minimum of two week supply and
- deliver within a very short time limit after receiving an order.

The remuneration system for pharmaceutical full-line wholesalers in most European countries is based on a margin, regulated by the individual Member State. This system enables pharmaceutical full-line wholesalers to purchase, store, handle and deliver low priced medicinal products in exactly the same quality and frequency as high priced products. Thereby, higher priced products cross-subsidize the storage, handling and distribution of lower priced medicinal products in order to ensure the continuous availability of all medicines. This also ensures that all medicinal products are treated in terms of safety and integrity at the very same high quality levels, irrespective of their value.

The products handled by pharmaceutical full-line wholesalers can be divided into an "attractive product segment", characterized by high margin, high volume and fast moving products and an "unattractive product segment", characterized by low margin, low volume and low rotation, which is cross subsidized by the attractive products.

If the revenue generating products' leave the full-line distribution channel, the current system will no longer be sustainable as it will not be feasible to handle the large number of products, which do not contribute to the coverage of fixed costs for pharmaceutical full-line wholesalers. Pharmaceutical full-line wholesalers will be left with the unattractive product segment to distribute, which is economically not viable, as cross subsidization cannot be applied any more.

In countries with public service obligations as described above, when placed on the wholesalers, the distribution system is streamlined, 'cherry picking' is not possible and a significantly decreased number of potential entry points for counterfeit medicines can be seen. For this reason, there is a correlation between the way the distribution chain is organised and the number of counterfeit medicines, which have been detected. The obligation placed on a wholesaler to carry the full range of products required in its geographical area of activity enables pharmacies to source all products necessary to serve patients from a single, safe and reliable source without having to contact several different supply sources. Thereby, the risk for counterfeit medicines' entering the legal supply chain is minimised through a streamlined, reliable supply chain.

Furthermore, Article 81(2) of Directive 2001/83/EC on the Community code relating to medicinal products for human use provides that *"the holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities,* ***ensure appropriate and continued supplies of that medicinal product to*** *pharmacies* ***and persons authorised to supply medicinal products,*** *so that the needs of patients in the Member State in question are covered. The arrangements for implementing this Article should, moreover, be justified on grounds of public health protection and be proportionate in relation to the objective of such protection, in compliance with the Treaty rules, particularly those concerning the free movement of goods and competition.".*

The purpose of the provision is firstly to place a joint responsibility on pharmaceutical manufacturers and wholesale distributors (wholesale operators of the distribution chain), in order to ensure the supply of medicines through pharmacies and persons authorised to supply medicinal products to the patients in a Member State. Secondly, this includes an obligation of manufacturers to distribute medicines to persons authorised to supply medicines (i.e. wholesalers). This provision should be strengthened as it is often overlooked in practical terms, when implemented into national legislation. Full-line wholesalers cannot fulfil this responsibility without receiving the medicines from the manufacturers.

It is therefore necessary to ascertain that pharmaceutical wholesalers are able to fulfil their responsibilities, by ensuring that manufacturers supply the medicines placed on the market to wholesalers to provide a safe and continuous single source of supply to pharmacies. Potential shortages, delays in supply and the necessity to screen a range of supply sources can thereby be avoided and safety and security of the supplied medicines significantly strengthened.

Member States should have implemented the provision above into the national legal orders before 31st October 2005. However, to date, the majority of the Member States have not adequately implemented this provision.

The uninterrupted supply of medicinal products to the patients is of paramount importance to deter pharmacies and patients from sourcing their medicines from other channels.

GIRP would therefore recommend a revision of Article 81(2) Directive 2001/83/EC, as amended by Directive 2004/27/EC, to include a European Framework for Public Service Obligations for wholesaling operators of the distribution chain.

GIRP would recommend the follow revision to Article 81(2):

"The holder of a marketing authorisation for a medicinal product and the wholesale operators of the distribution chain shall, within the limits of their responsibilities, ensure the supply of the said medicinal product actually placed on the market in a Member State to pharmacies through wholesale operators of the distribution chain, to cover the needs of patients in the Member State in question.

The arrangements for implementing this Article should, moreover, be justified on grounds of public health protection and be proportionate in relation to the objective of such protection, in compliance with the Treaty rules, particularly those concerning the free movement of goods and competition."

Naturally, a short, streamlined supply chain with clearly defined responsibilities provides a high degree of security and strengthens the integrity of the supply chain. Our recommendation for a revision of Article 81(2) Directive 2001/83/EC as amended by Directive 2004/27/EC to include a European Framework for Public Service Obligations for the supply chain partners will have a direct impact on patient safety by further securing the distribution chain for medicines as it enables authorities to control, without impacting on competition rules, the number of operators in the supply chain. This would in turn limit the number of operators and persons allowed to intervene in the supply chain.

b. Licenses for non wholesaling operators of the distribution chain

All non wholesaling operators of the distribution chain (i.e. logistics providers) are not specifically licensed according to any specific licensing systems for pharmaceutical products in the Member States in which they are established. Their activities are normally supervised by the manufacturers, however they should meet established regulations which set forth strict minimum requirements for pharmaceutical product storage and security, as well as for the treatment of returned, damaged, recalled and outdated products.

If non wholesaling operators carry out their activity under the responsibility of the marketing authorisation holder, the marketing authorisation holder is responsible for the compliance of the operator with GDP provisions. Common licensing requirements and renewal schedules should be established and also include the introduction of a 'sunset clause' in case of inactivity for a certain period of time.

c. Licenses for other operators

While other operators (as described above) neither hold proprietary rights over the products they trade, nor are they directly involved in their storage or distribution, they should be licensed through a regulated framework and subjected to stringent standards and enforcements. Currently, these operators are often not known and exist without any controls. Information on the holders of a license regarded as 'other operators' should be accessible for all parties in the supply chain.

d. Licenses for the sale or supply of a medicinal product for the purposes of export

The sale or supply of a medicinal product for the purposes of export is amongst some of the activities occurring within the distribution chain which are often exempted from licensing requirements. In this respect, GIRP is aware of one particular example. In the UK the sale or supply of medicinal products for the purposes of export is one of the activities which are covered by an exemption within existing legislation.

Section 48 of the UK Medicines Act 1968 postponed the requirement to hold a license for such activity. This essentially means that any person or company can purchase pharmaceutical products from any other person or company in the UK (or anywhere else in the EU) as long as it is "for the purposes of export" and is thereby exempted from obtaining a license for this activity.

Therefore, the purchase request from any company to another wholesaler or manufacturer only requires the words "for the purposes of export" to be stated on it (the order), to fall within the exemption from licensing. While the exemption under Section 48 UK Medicines Act 1968 only applies to the final exporter, all trade up to the exporter will need to be licensed. It is however imperative that such activities fall clearly within the scope of a regulatory framework. Currently, as this is not a licensable activity, therefore the number of companies operating in this way cannot be ascertained.

4.2. Tightening rules on inspections, regular audits of GMP/GDP compliance and increased transparency

4.2.1. Harmonised provisions for inspections by competent authorities of parties in the distribution chain

Key ideas for changes to EC legislation submitted for public consultation

a. Include specific harmonised provisions for inspections by competent authorities of parties in the distribution chain (e.g. wholesalers, brokers, traders, agent, business-to-business platforms). b. Require GDP certificates to be issued after each inspection of a wholesaler.

a. Harmonised provisions for inspections

The fight against counterfeit medicines can only be successful, when the operators within the legal supply chain are supported by an effective harmonised regulatory framework, which is properly supervised and enforced. In respect of the tightening of rules on inspections on all parties in the distribution chain further legislative measures will be required.

In the light of the current divergence surrounding the issuing of licenses for those involved in the distribution chain in Europe (as described before,) there is no solid or harmonised basis to rely on the same high standards for inspections by the competent authorities of the Member States of the operators involved in the distribution of medicines. Therefore, GIRP fully agrees with the key idea presented in the consultation document.

Following the establishment of a classification system for the issuing of licenses, specific harmonised provisions for inspections by competent authorities of all actors involved in the distribution of medicines (e.g. wholesaling operators of the distribution chain, non wholesaling operators of the distribution chain and other operators) should be established.

In this respect – in contrast to GMP, which are enforced by a Directive – the implementation of the GDP Guidelines into national law is not an obligation for Member States and it is hard to foresee when and in which way revised GDP Guidelines would be implemented in the Member States' legislative framework. However, GIRP has carried out a survey amongst its members on the level of implementation of the current GDP Guidelines. The result was satisfactory, concluding that EU Member States have implemented the GDP Guidelines into national law. Despite this fact and in order to ensure a harmonised standard of implementation as well as the fast and complete implementation of new provisions combating a possible entry of counterfeit medicines in the legal supply chain, the European Commission might envisage including provisions on this subject through a revision of Directive 2001/83/EC.

GIRP strongly supports the setting of specific harmonised provisions for inspections by the competent authorities of the Member States in which all parties involved in the supply of medicines are covered. Specific harmonised provisions for inspections by competent authorities of all parties involved in the distribution chain should be equally specified in a revision of Directive 2001/83/EC.

The language of the preamble of the European GDP Guidelines could be used as a basis for creating such harmonised provisions for the inspections of wholesaling operators, as well as non wholesaling operators of the supply chain, when reflected in the pharmaceutical legislation.

To this end the preamble of the European GDP Guidelines reads: *"The Community pharmaceutical industry operates at a high level of quality assurance, achieving its pharmaceutical quality objectives by observing Good Manufacturing Practice to manufacture medicinal products which must then be authorised for marketing. This policy ensures that products released for distribution are of the appropriate quality. This level of quality should be maintained throughout the distribution network so that authorised*

medicinal products are distributed to retail pharmacists and other persons entitled to sell medicinal products to the general public without any alteration of their properties. The concept of quality management in the pharmaceutical industry is described in Chapter I of the Community Guide to Good Manufacturing Practice for medicinal products and should be considered when relevant for the distribution of medicinal products. The general concepts of quality management and quality systems are described in the CEN standards.

In addition, to maintain the quality of the products and the quality of the service offered by wholesalers, Directive 92/25/EEC (insertion added: now amended by Directive 2001/83/EC as amended by Directive 2004/27/EC) provides that wholesalers must comply with the principles and guidelines of good distribution practice published by the Commission of the European Communities.

The quality system operated by distributors (wholesalers) of medicinal products should ensure that medicinal products they distribute are authorised in accordance with Community legislation, that storage conditions are observed at all times, including during transportation, that contamination from or of other products is avoided, that an adequate turnover of the stored medicinal products takes place and that products are stored in appropriately safe and secure areas. In addition to this, the quality system should ensure that the right products are delivered to the right addressee within a satisfactory time period. A tracing system should enable any faulty product to be found and there should be an effective recall procedure."

In every case a provision requiring a 'state of the art" interpretation of GDP Guidelines should be foreseen in legislation. However, other provisions will need to be established for other operators who have no physical contact with medicinal products.

b. Certificates to be issued after each inspection by the health authority of an operator of the supply chain

GIRP firmly believes that a regular review of all license holders with respect to compliance to their respective standards (GMP for manufacturers including GDP for direct distribution, GDP for wholesaler and non wholesaler operators of the supply chain as well as another specific certificate, such as good commercial practice for other operators) throughout the European Union is essential to ensure the safety of the legal supply chain. In order to obtain and keep a license, full compliance with the Guidelines on Good Distribution Practice Guidelines (94/C 63/03) or a respective set of Good Commercial Practice guidelines must be regularly checked and controlled by the authorities of the Member States. Certificates should then be issued after each inspection of a properly licensed operator of the supply chain.

However, there must be the appropriate strengthening of current GDP certification systems for wholesaling and non wholesaling operators of the supply chain. Certification must be transparent to business partners, to authorities and to health professionals. This certification must be properly and effectively provided by the competent authorities in charge of the licensing and regulation of the distribution chain, equally enforcing GDP and other appropriate standards for other operators. Enforcement can ensure that all in the

supply chain are dealing only with certified partners, i.e. those approved and licensed by the competent authorities. Thus, the authorities, industry and the supply chain can work in partnership to ensure supply chain integrity, which is the crucial pre-requisite of an effective anti-counterfeiting strategy in the medicines' market.

Non GDP compliant operators, as well as those which do not comply with their respective licensing requirements should be provided with a time frame for providing proof of their compliance as otherwise their license should be revoked. The same strict requirements should also apply for manufacturing authorisation holders, who distribute their own products as well as for other operators.

All parties in the supply chain should only work with certified partners as a standard harmonised practice. Specific attention should be given to the role and licensing of distribution operators regarded as vulnerable entry points of counterfeit products into the supply chain as well as other operators in the supply chain who would not qualify for a GDP certificate due to the fact that they do not physically handle pharmaceutical products.

4.2.2. Regular audits of all operators involved in the medicines supply chain

Key ideas for changes to EC legislation submitted for public consultation

Make regular audits of GMP/GDP compliance mandatory by qualified auditors
- of (contract) manufacturers by manufacturers;
- between suppliers (wholesalers, manufacturers) at least in cases of suspicion of non-compliance with GMP and/or GDP.

Firstly, it is imperative to stress that certification (GMP, GDP or other) should be a pre-requisite for the granting of a license to any operator that is involved in the distribution of medicinal products. Furthermore, the passing of regular compliance inspections must be a pre-condition for any operator to retain an already granted licence. With respect to compliance to GDP requirements the certification and regular inspection should be carried out by health authorities.

Secondly, in cases of doubt of non-compliance with GMP and/or GDP supplier audits offer an additional mean of ensuring that the operators of the supply chain deal with reliable partners, which usually should be ensured by consulting the respective GMP, GDP databases (or equivalent database for other operators) concerning the validity of the license prior to taking up business relations with a supplier/wholesaling operator/non wholesaling operator/ other operator of the supply chain.

Already today, based on a risk assessment, GIRP members carry out supplier audits in accordance with their own specialised internal auditing processes. Supplier audits serve as an additional layer of security in cases of doubt or concerns, before starting a business relationship with a new supplier, who is then thoroughly and systematically screened.

4.2.3. Increased transparency for all actors involved in the distribution of medicines through a Community database

Key ideas for changes to EC legislation submitted for public consultation

Establish a Community database of wholesalers (including distributing manufacturers) documenting GDP compliance. This could be achieved via extension of the EudraGMP database.

A Community database for licensed actors of the supply chain

In practice, GIRP can confirm that pharmaceutical full-line wholesalers currently verify the reliability of their (wholesale) suppliers by requesting a copy of the wholesale license. However, there is still the theoretical risk that such a license is equally counterfeited. A secured, centralised, online database with public access, containing information on authorisations and GDP/GMP certificates of wholesalers and manufacturers, as well as all other operators involved under their respective licenses, would provide a much better and safer tool to ensure that only licensed partners interact with each other. At the same time, the obligation of each supply chain operator to verify the compliance of its partners should be compulsory.

GIRP strongly supports the idea of an obligation to maintain an online, real-time database on a European level for manufacturing and distribution licenses holders and documentary evidence of GDP compliance, as well as evidence of compliance of the other operators to an established set of good commercial practices for other operators. This could happen through a single point of contact in each Member State, which then submits all information on the license holders, to a central European point, ideally located at the EMEA, in order to allow authorities, customs and police officials, as well as the supply chain partner's permanent up-to-date access to this information.

This could be done in exactly the same way as the current project of a database for manufacturing authorisation holders "EudraGMP", which is currently on the way at the EMEA.

On the other hand it is very important for pharmaceutical full-line wholesalers to verify the GMP compliance of manufacturers and importers in the EU.

In this respect GIRP, strongly embraces the establishment of the "EudraGMP" database[7], serving as a single point of contact to obtain all necessary information on manufacturing and import authorisations issued by EEA competent authorities, GMP certificates and non-GMP compliance information.

Pharmaceutical full line wholesalers should receive full read access to the EudraGMP and a future GDP database, in order to ensure the validity of GMP and GDP compliance of the

[7] See information on the "EudraGMP" database of the EMEA under http://www.emea.europa.eu/Inspections/EudraGMP.html.

manufactures and importers of medicines they distribute as well as other wholesalers in order to be alerted in case of suspected non-GMP or non-GDP compliance and suspension and/or revocation of a license. The objective of these databases should be to establish a framework which ensures that all operators in the supply chain only buy and sell from and to certified sources, thereby safeguarding the health and well-being of European citizens.

Additional efforts should be put into a central database comprising all operators dealing with medicines, which are subject to a different license (non GMP/GDP) as they are not physically in control of the medicines.

We highly appreciate that the GMP database once finalised will be publicly available. However, we would like to stress that in case problems with licenses are not publicly accessible, it is crucial that wholesalers are aware of such problems and therefore need access to all information related to safety or security issues of GMP/GDP license holders in the database.

4.2.4 Only buy from and sell to authorised and certified sources

GIRP strongly recommends that all supply chain operators should commit to **only buy from and sell to authorised certified sources**. Stricter enforcement procedures can ensure that all in the supply chain are dealing only with "certified operators".

Authorities, industry and the supply chain can work in partnership to secure supply chain integrity, which is the crucial pre-requisite of an effective anti-counterfeiting strategy in the pharmaceutical market. Doing "Business with Certified Partners Only" should become the standard harmonised practice.

4.3. Tracking and Tracing

4.3.1. Background and Pre-Conditions

Pharmaceutical full-line wholesalers have to employ state-of-the-art information technology and physical infrastructure to undertake their services with the current level of intensity, sophistication, quality and efficiency and operate quality systems which guarantee proper conditions of medicinal products and the safe, fast, continuous and secure delivery of medicines within the pharmaceutical supply chain.

Pharmaceutical full-line wholesalers face the logistical challenge to ensure just-in-time delivery to pharmacies and hospitals and therefore operate under most complex organisations, using sophisticated IT systems in order to guarantee the continuous just in time supply of all medicines to the patients in Europe. In this respect delivery times are very short and the speed of commissioning and delivery are crucial in order to be able to maintain patients' safety.

The enormous and very complex throughput in wholesalers' warehouses (up to 12 packs per second, with an average order fulfilment time of less than an hour) requires a high speed of action.

Concerning the tracking and tracing of medicines there is no uniform approach on how to track and trace the flow of medicines in Europe today, due to the lack of standardised product identification structure and the diversity of carriers, which are used in coding systems that national regulatory bodies are supporting actively, because their own monitoring systems are built up on this basis.

Some EU Member States have started to introduce national legislation for the tracking and tracing of medicines, which are very country specific and do not contribute to find a global or European solution to the problem. It is important to note that these national systems are all different without any European harmonization.

Harmonised, machine readable data is essential to automatically capture the relevant product information within the workflow in the warehouse. Therefore, wholesaler require in addition to the information necessary for the pharmaceutical industry:

- National product identification number
- Expiry date and
- Batch number

in a machine readable format on every pack as a pre-requisite to start reflecting on the implementation of tracking and tracing procedures.

After an evaluation of the various technology options, GIRP believes that for the present a 2D code, for example the data matrix code, is the most promising solution with regards to code labelling, as it allows further content expansion on smaller space and may also cover additional information needs of manufacturers.

In the future, Radio Frequency Identification technology (RFID) and its tags as carriers may probably allow the supply chain operators to automatically identify products. However, even though RFID could bring significant advantages to tracking and tracing of medicines and to the identification of counterfeited products, it has presently proven not to be a technology mature enough to be embraced on the short run. Due to current technical difficulties in respect of reading inaccuracy with aluminium, glass and/or liquids (which may be even altered), GIRP considers RFID to be a solution for the future only.

Overall, pharmaceutical full-line wholesalers require a solution which is suitable for the pharmaceutical supply chain, allowing:

- smooth integration of national product identification, expiry date and batch number
- to keep up the speed of delivery
- European wide technological harmonisation and
- Implementation at competitive costs.

A harmonized coding and identification system is a pre-requisite for the reflections below.

4.3.2. Centrally accessible record to facilitate traceability of batches throughout the distribution chain

Key ideas for changes to EC legislation submitted for public consultation

Require the possibility of tracing ownership and transactions of a specific batch. This should be achieved by making a specific record (pedigree) obligatory. The record should be accessible by all actors in the distribution chain.

As there is no uniform approach on how to deal with the flow of medicines throughout Europe, due to the lack of harmonised, machine readable information on the products, batch tracking is not readily feasible.

It is also important to stress that currently many pharmaceutical full-line wholesalers do not operate automated reading systems, which would be required to carry out batch tracking and which are a pre-requisite to maintain the delivery frequency to supply medicines in a timely manner.

In addition, GIRP would like to emphasize that there will be a decrease in the speed of commissioning in the warehouses and delivery to the retail outlets, related to the recording of all batch numbers for the outgoing medicinal products and current systems are not yet adapted for high numbers of different medicinal products (up to 100,000 different products).

GIRP would like to stress that the complexity of implementing a full batch traceability system offers no real direct result in terms of patients' safety. Bearing in mind the objectives of the European Commission on assessing key ideas for the better protection of patients against counterfeit medicines it is important to distinguish between measures which are results orientated and measures which are process orientated. GIRP believes that the introduction of a pedigree at the batch level is a process oriented measure and does not lead to the desired results in terms of value for patients' safety.

However, a possible short term option would be the implementation of a DESPATCH ADVICE (DESADV) system. This system is widely and successfully used in other sectors.

At the manufacturer or pre-wholesaler level, each time a supply request is to be fulfilled, the dispatcher would inform the consignee of an incoming delivery via a Dispatch Advice (avis d'expédition in French) in the form of an electronic notification in accordance with EDI standards.

The DESADV, as it has been modified and updated by the CIP in France (a professional organization working on common standards and procedures), contains a thorough description of the delivery (identity of the logistic party if applicable, number and content of pallets, number and content of cartons, number and price of products and batch numbers).

Upon receipt at the goods incoming area, staff would be able to verify the DESADV notification against the actual delivery. This would enable licensed operators in the distribution chain to authenticate the delivered batches.

If such a process was implemented, pharmaceutical wholesalers could, in return, immediately inform manufacturers via EDI of a possible problem in case of mismatch.

4.3.3. Mass serialisation for pack-tracing and authenticity checks on a case by case basis

Key ideas for changes to EC legislation submitted for public consultation

Require the possibility to trace each pack and perform authenticity checks. This could be attained by a mass serialisation feature on the outer packaging. Technical details would be further defined in implementing legislation and/or by standardisation organisation.

As previously described, the introduction of a harmonised product identification and coding system is a pre-requisite to track and trace medicines. This necessity has been recognised in several Member States and numerous initiatives have been developed, resulting in national "island" solutions, without view towards a homogeneous solution on European level.

In order to find a solution to halt the developments of national 'island' solutions it is essential to work towards a European harmonised coding and identification system. In this respect, the European Federation of Pharmaceutical Industries and Associations (EFPIA) is preparing to launch a pilot project on mass serialisation (2D bar code).

GIRP is fully supporting this initiative, which has - as the essential first step – started its work with the elaboration of a harmonised 2 D bar code, carrying a randomised, individual number for every pack and including all information requirements of the distribution chain, such as the inclusion of the national identification number, the batch number and the expiry date. The first phase of the project foresees the authentication of the product at the pharmacist, at the point of dispense to protect the patient from being dispensed a recalled, expired or counterfeited medicine. To provide the necessary layer of security at the distribution level, wholesalers can authenticate products in case there is a doubt if they are genuine and can verify the authenticity of returned medicines. GIRP and its members believe that this initiative takes a realistic approach to protect patients from counterfeit medicines with a view to the current technical feasibility and the involved costs. Today, there is no technology on the market, which allows the automatic scanning of every pack of medicine. Therefore with current technology it is not feasible to track and trace individual medicines' packs on a larger scale. The initiative presented by EFPIA takes this fact into account as wholesalers can authenticate products either in the goods incoming area, where commissioning and deliveries are not slowed down or a the medicines return area to verify that no counterfeit medicines are entering a warehouse through returns.

Regarding the ideas outlined in the consultation paper of European Commission to limit the number of products, which should be tracked and traced on item level GIRP would like to stress that the constraints outlined above concerning the feasibility of such a process remain fully valid in case a large number of products are affected or the concerned products are sold in large quantities.

Pharmaceutical full-line wholesalers would like to emphasize that there will be a significant decrease in the speed of commissioning and delivery in the warehouses, related to the scanning of individual medicines during commissioning, which increases with the number of different products and their volumes as the necessary technology is not available yet. Once on the market, the implementation of this technology will require significant investments and increase the costs of medicines distribution. However, concrete assessments of the involved investments cannot be carried out at the moment, due to the lack of marketable technology (even pilots have not been carried out so far).

Brussels, 9th May 2008

Annex 1

Country	Public service obligation	GDP implemented		Pharmacist as qualified person		Qualifications of the qualified person
		Yes	No	Yes	No	
Austria	**no**	✓		✓		1 pharmacist per company
Belgium	**yes**	✓		✓		1 pharmacist per warehouse; max. 5 warehouses per pharmacist, no legal obligation, but agreement with the government
Czech Republic	**no**	✓		✓	✓	5 different professions allowed: pharmacist; doctor; veterinarian; chemist; chemical engineer; natural scientist
Denmark	**not yet implemented**	✓			✓	Management representative with defined authority and responsibility, in order to ensure that a quality system is in implemented and maintained. The person shall be appropriately qualified. Danish Medicines Agency needs to evaluate and approve the specific person, if the person does not hold a pharmacy degree.
Estonia	**yes**	✓		✓		The wholesalers on the market must have pharmacists as qualified persons. The qualified person needs to get approved by the authority.
Finland	**yes**	✓		✓		
France	**yes**	✓		✓		A pharmacist has to be on the Board of the wholesaling company and 1 pharmacist has to be the responsible person in each warehouse
Germany	**no**	✓			✓	The qualifications of the responsible person of the warehouse have to be individually proven to and confirmed by the authority
Greece	**yes**	✓		✓		
Hungary	**no**	✓		✓		
Ireland	**not yet implemented**	✓			✓	No specific qualifications for the responsible person, but it must be a person approved by the IMB, the Irish Medicines Board
Italy	**yes**	✓		✓		1 pharmacist per warehouse

Lithuania	**yes**	✓		✓		Qualified person must be approved by the Lithuanian State Medicines Control Agency and must have at least 2 years per 10 years experience in wholesale's company
Luxembourg	**not yet implemented**	✓		✓		1 pharmacist per warehouse
Netherlands	**no**	✓		✓ (until 2007)	✓ (since 2007)	qualified person for the specific tasks, as judged by the wholesaler
Norway	**yes**	✓		✓		
Poland	**no**	✓		✓		min. 1 pharmacist per warehouse plus 1 pharmacist per special group of products: psychotropics, narcotics, etc.
Portugal	**yes**	✓		✓		
Romania	**yes**	✓		✓	✓	One warehouse must be run by a pharmacist. However, in addition, there is the qualified person, which does not necessarily need to be a pharmacist, but can also be a chemist, medical doctors or biologist, but have to be accredited by the National Medicines Agency.
Slovakia	**no**	✓		✓		
Slovenia	**no**	✓		✓		
Spain	**yes**	✓		✓		1 pharmacist per warehouse, sometimes even 2 or 3 per warehouse necessary
Sweden	**no**	✓			✓	The 2 wholesalers on the market both have pharmacists as qualified persons, however, this is not a legal requirement. The qualified person needs to get approved by the Swedish Medical Products' Agency.
Switzerland	**no**	✓		✓		1 pharmacist per warehouse
United Kingdom	**no**	✓			✓	qualified person must have min. 2 years of experience in a senior position; 1 qualified person per warehouse