

EFPIA RESPONSE TO

The European Commission 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

I. Introduction

EFPIA welcomes the opportunity to take an active part in the consultation process with a view to assessing the need for action by the European Commission with respect of changes to EC legislation in a number of areas. EFPIA believes that decisive and urgent action is required to enhance product security in order to protect European patients and would welcome new EU legislative initiatives in this area.

II. General comments

Broadly speaking EFPIA supports the Commission's overall approach and the set of concrete measures proposed to address the problems related to counterfeit medicines in Europe.

In addition to the input already provided in April 2007 to Part I of the Consultation on Combating Counterfeit Medicines as well as the input provided in April 2007 and October 2007 on Part II of the Consultation 'Safe Medicines in Parallel Trade', this paper provides a detailed response to each set of key ideas proposed in the consultation.

However, EFPIA would like to stress that the proposed measures should be considered as a whole rather than individually or 'a la carte' (i.e. 'cherry picking'). The proposed set of key ideas should therefore be considered as part of a comprehensive strategy focused on ensuring that only safe products reach the patient (i.e. ensuring the integrity of the pack content) as well as on strengthening the integrity of the supply chain. A number of additional measures have also been proposed in order to address the different aspects of this serious criminal activity.

1. Securing supply of safe products

EFPIA believes that the number one focus of the legislative reform should be to ensure that the integrity of the original package is absolutely guaranteed throughout the entire supply chain, from the time it leaves the original manufacturers' hands to the point that it reaches the end user.

In order to achieve this, there are three core elements for an efficient technological anti-counterfeiting strategy that would help to ensure the integrity of the packs' content.

- Use of tamper-evident packaging¹ on all products

EFPIA fully supports the proposed measure in section 4.1.3 requiring the use of tamper-evident packaging and believes that this measure should be extended to all prescription pharmaceutical products rather than on a risk-based approach only as counterfeiters will simply move into products, which are not subject to such measures.

- Use of overt and covert authentication² features

Technology choice should be specific to each manufacturer (diversity is necessary in order to reduce risk of copying).

- Strengthening product identification at individual pack level through a harmonised coding standard as proposed in section 4.1.5

This is best achieved by implementing an end-to-end product verification system of each individual unit at the point of dispensation (i.e. pharmacy) rather than a full track and trace system such as a pedigree. Harmonization of the coding rules across Europe is essential in order to guarantee a safe supply chain.

The above-mentioned measures aimed to guarantee the integrity of the contents of the pack assume a ban on repackaging³ at a European level.

2. Strengthening the integrity of the supply chain

- Ban on repackaging as proposed by section 4.1.3

If products are repackaged, other than by the original manufacturer, the MA holder of the original product or a third party contracted to repack by the original manufacturer or MA holder of the original product, any anti-counterfeit features incorporated into the original packaging are rendered ineffective. This makes it more difficult to detect counterfeits.

- Auditing of the supply chain as proposed by section 4.1.1 b

While basic regulations exist to prevent traders, brokers or agents from causing safety problems, these need to be more strictly enforced. As a general principle, the shorter the supply chain, the more secure it will be.

The current system of GMP (Good Manufacturing Practices) audits should be extended to GDP (Good distribution Practice) audits as well as to the entire supply chain in order to assure that measures taken with respect to product protection, packaging practices and distribution practices are properly used and followed.

- Clarifying the liability of traders, brokers or agents as proposed by section 4.1.1 a

¹ Tamper-evident packaging: packaging feature or design allowing visible evidence/recognition by the actors in the supply chain or by the patients when the packaging has been opened (packaging destruction)

² Authentication is defined as a control operation based on the recognition of overt and covert authentication features (e.g. use of holograms, colour shifting inks or taggants) providing the guarantee that the product is genuine.

³ By repackaging, we mean any form of relabelling (overstickering), reboxing, rebranding, etc, as per the ECJ case-law.

The current system - and the way the legislation is applied - brings confusion as to who is liable for the product in case of product damage or recall control. Furthermore, there are various shortcomings in the way the notification procedure operates in case of imports by any distributor not being the marketing authorization holder (as foreseen by Article 76 of EC Directive 2004/27/EC) since EFPIA is aware that not all distributors comply with the existing procedures for notifying the EMEA in the case of the distribution of centrally approved products. Traders, brokers, agents, distributors and retailers of over-the-counter and prescription medicines should be subject to strict liability rules for the sale of their products, including wrong product information leaflets. This would provide further incentives to increase the integrity of the legitimate supply chain and would allow market forces to find additional solutions to tackle the problem of counterfeits.

- Notification of corrupt products

Where a patient, pharmacist, wholesaler, trader, broker or agent reports a problem with a product believed to have been corrupted (suspicion of counterfeit product or product damage), there should be a means of ensuring that the person in the supply chain who receives the information (wholesaler, trader, broker, agent, wholesaler or pharmacist) duly informs the health authorities, who in turn should inform the manufacturer. This can be achieved through the web based end-to-end verification enabled by the mass serialisation of all products as suggested by section 4.1.5.

3. Complementary measures

To combat the counterfeiting of medicines, it is necessary to address the different aspects of this serious criminal activity. In addition to the areas where the Commission has expressly identified and proposed a list of possible legislative changes, the industry feels that there are other areas, which require serious consideration and action on the part of the Commission.

We would like to take this opportunity to urge the Commission to take additional measures to address the counterfeit medicines problem more holistically. A coordinated effort of all the different public and private stakeholders involved is necessary to put in place the national and international strategies aimed at combating counterfeit medicines. We would invite the Commission to consider the following complementary measures and proposals:

- Criminal sanctions

Over the years, pharmaceutical companies have repeatedly expressed the need for heavier and exemplary criminal sanctions to act as a deterrent against the serious crime of counterfeiting medicines. This was advocated in EFPIA's response to the Commission Green Paper on Combating Counterfeiting and Piracy in the Single Market in January 1999.

The penalties for counterfeit drugs must be at least as strong as those for narcotic drugs to provide a disincentive for the illegal drug traffickers to switch from cocaine, for example, to dealing in fake prescription drugs. Criminal penalties are particularly important in the medicines' sector due to the foreseeable harm caused to human health and safety. For this reason, we are anxious that progress be made with the proposed directive on criminal sanctions

for the enforcement of IP rights (DG Justice Freedom and Security), which has been stalled since April 2007. We would like to see the adoption of more severe penalties than those proposed in the Directive, in line with those for illegal drugs.

- Tackling sales of counterfeits over the internet

The sale of counterfeit drugs over the Internet is a critical and growing problem in Europe, which needs to be addressed. It is now well established that most drugs offered via illegal Internet pharmacies represent a risk to the patient. Discussions are taking place on how to raise public awareness of the problem in an appropriate and productive way.

EFPIA believes that both public health authorities and pharmaceutical companies have an important role to play in educating consumers on the risks posed by counterfeit medicines. Action in this area could influence the “demand” side, one important issue that is currently missing from the proposals. A pan-European license system with authorised Internet pages for Internet pharmacies should be envisaged.

- Proper law enforcement

The proposed controls will require proper law enforcement, which in turn will require significant additional regulatory resource for Member States. If there is not comprehensive and proper enforcement, there is the possibility that less scrupulous operators will continue to by-pass regulations and the burden of the increased regulation and control will fall on the bona fide operators with no commensurate decrease in the risk to patients. It should not be the role of industry to act as “surrogate” enforcer in place of the regulatory authorities. Law enforcement measures, such as the removal of licences (closure of factory or of import businesses), must also be considered because current inspections by regulators apparently do not act as a sufficient deterrent. In addition, EFPIA proposes remedies like seizure and destruction of the production/distribution equipment (machines, transport vehicles, etc). Continued education of the enforcement authorities, coupled with sufficient and dedicated resources, would help alleviate the problem.

- International enforcement

Treaties for international enforcement of judgments are also desirable to prevent these criminals from moving from one country to another. EFPIA would also like the Commission to consider how it could use influence to support countries outside the EU where counterfeit medicines may originate to minimise the impact of this illegal activity. EFPIA realises that the responsibility for the various elements mentioned here lie with different DGs in the Commission so inter-DG cooperation and exchange of information will be necessary.

III. EFPIA specific input to proposed key ideas by section

Section 4.1: Tightening requirements for manufacture, placing on the market of medicinal products and inspections

4.1.1. *Subject all actors of the distribution chain to pharmaceutical legislation*

Key ideas for changes to 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

b) 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.

EFPIA position:

EFPIA fully supports the proposed key ideas listed under section 4.1.1.

Rationale:

- Any supply chain control has to be audited⁴ to ensure that the implemented measures are working in the desired way. Traders, brokers and agents are not currently inspected by regulators.
- There should be a legal framework for appropriately extending GMP auditing system to include auditing of the whole supply chain. In this respect, EFPIA is supportive of the need for a harmonized EU framework to avoid different approaches by national agencies and ensure predictability of operations for the global industry.
- To ensure downstream suppliers comply with the same obligations as wholesalers, the responsibility of all players should be the same as that applying to wholesalers, not just similar, except where this would not be relevant. For example, the provisions on receiving goods, storage conditions, etc., are not a priori relevant to a broker.
- The existing GMP and GDP could work as an adequate basis for this. The suitable starting point of any supply chain control should be at the drug product manufacturer's level as there are GMP certificates available, quality systems in place, as well as established control of all incoming starting materials such as actives, excipients, packaging materials and security features.
- For audits of the distribution chain, companies should have the option of using their own personnel or accredited auditors. The minimum qualifications and

⁴ Inspections are conducted by regulators, whereas audits are conducted by industry.

experience for “qualified auditors” should be defined. Harmonised GDP guidance and mutual recognition of standards for qualification should be sought across the EU. For consistency of operating, the mandatory application of Community procedures on inspection and supervision should be applied so that all Member States operate in a harmonised and predictable manner. This harmonization may also facilitate mutual recognition of inspections by competent authorities in other Member States and third countries as deemed appropriate.

- National health agencies should be entitled to perform “supply chain security inspections” along the whole supply chain from manufacturer to the point of dispensing and customs should be included in the regular quality inspection plan of the supply chain.
- A legal basis for “supply chain security inspections” should be created in analogy to GMP audits. In this respect, the WHO’s newly drafted “Good Distribution Practices” could be used and be supplemented by specific requirements for combating counterfeits.
- Manufacturers need to work together with the authorities, as in GMP, because companies cannot do the audits alone. Traders, brokers and agents cannot audit each other because they are not experienced to do so. The national health agencies could have shared responsibility with manufacturers (as with and based on GMP) but currently they do not feel responsible for this. There is a need for a collaborative core of inspectors to join forces, possibly within the WHO/ IMPACT.
- In the event of non-compliance, a competent authority should be granted powers to immediately demand a cessation of operations by the non compliant party, until it can be confirmed that such non compliance has either been rectified, or the party in the distribution chain has their license to operate withdrawn. This competent authority should also have the power to seize and destroy suspect product.
- In addition a legal basis for supply chain security audits at manufacturers of printed pharmaceutical packaging material should be created. The WHO’s drafted “Good Security Practices” for printed pharmaceutical packaging material could be used as a basis for audits at printed packaging material manufacturers.
- The current system of GMP inspections / audits should be extended to GDP (Good distribution practices) inspections /audits to ensure that the measures taken for product protection, packaging practices and distribution practices such as tracking and tracing, pedigrees, etc, are properly used and followed.
- The WHO/IMPACT “Draft Principles and Elements for National Legislation against Counterfeit Medical Products” which aim to make all actors of the supply chain accountable is a good basis.
- If in a new business model where it is contemplated that the parallel trader will distribute product packs directly to the patient, will an exception apply on the basis of direct distribution to the patient?

4.1.2. Tightening rules on inspections

Key ideas for changes to EC legislation submitted for public consultation

- Strengthen provisions on inspections and supervisions, in particular regarding inspections in third countries. For example, make application of the Community procedures on inspections and supervision (“Compilation of Community Procedures on Inspections and Exchange of Information”) mandatory.
- Include specific harmonized provisions for inspections by competent authorities of parties in the distribution chain (e.g. wholesalers, brokers, traders, agents, business-to-business platforms).

EFPIA position:

EFPIA supports the proposed key ideas listed under section 4.1.2.

Rationale:

The supply chain control is most effective if the system is at least designed supra-nationally, so an international focus will be the most suitable.

To ensure wholesalers, traders, brokers, agents and downstream suppliers comply with the same obligations as manufacturers, specific harmonized provisions for inspections by competent authorities of all parties in the distribution chain should be included. In addition, a method of mutual recognition of inspections should be implemented across all inspecting bodies in the EU, to avoid duplication of inspections by multiple authorities and to lower costs. Any proposed amendment will need to be worded to cover all types of premises and a GDP certificate should be required for the simplest of operations (regardless of issues to do with “lack of patient harm or safety”). EFPIA believes that the European Medicines Evaluation Agency (EMA) should take a coordinating and accountable lead in implementing such a mutually recognized and efficient system of inspections.

Experience from EFPIA member companies shows that in certain countries the ability to differentiate between legitimate activities and illegitimate activities of certain parties in the distribution chain are very difficult to detect.

Inspections must preferably not be announced because the advance warning enables the actors of the distribution chain to conceal any elements of proof of illegal activities.

It will be important to define “competent authorities” because currently the ministries of health do not feel responsible for supply chain inspections.

4.1.3. Improving product integrity through a unique seal from the manufacturer to the retailer or wholesaler, using a risk-based approach, supported by a ban on repackaging

Key ideas for changes to EC legislation submitted for public consultation

Require the outer packaging of medicinal products to be sealed. This would reveal any subsequent opening of the packs.

Such a requirement could be applied to certain categories of products chosen on a risk-based approach, i.e. by taking into account the public health impact of the appearance of a counterfeit product and the profit strategies of counterfeiters.

The right to opening the outer packaging would be restricted to the market authorisation holder and end-user (hospital, health care professional, or patient).

EFPIA position:

EFPIA supports the proposed key ideas listed under section 4.1.3. EFPIA also believes that a risk-based approach is no longer appropriate since counterfeiters are now targeting a growing range of medicines and will simply move to target any weaknesses in the supply chain. EFPIA believes that the measures should be applied across the full range of medicines for human use requiring a prescription. Its implementation, however, may require a stepwise approach on the basis of risks until full coverage is achieved.

Rationale:

Research-based manufacturers are making important investments in anti-counterfeiting technologies to enhance the security of their products and ensure that the highest quality products reach the patient. These include a number of authentication technologies such as overt and covert features placed on the packaging, which are intended to guarantee that the pack is genuine. A full description of these features can be found in a report published by the WHO IMPACT report on 'Anti-counterfeiting technologies for the protection of medicines'⁵. In summary, these include holograms, optical devices, and security graphics, some invisible to the naked eye, placed on the original pack. These naturally rely on the original packaging remaining intact.

Companies have therefore developed as part of their respective anti-counterfeit strategies, a number of tamper evident container closure systems. These include:

- Tamper evident security seals and tapes that break and leave a visible trace when someone first opens the pack;
- Packaging techniques with perforated boxes, which must be ripped in order to open the box. This allows the option to close up the box once it has already been opened while still making any initial tampering evident;
- Special glue for the flaps, which must also be ripped open but which does not allow the box to be closed again. However, this is often combined with perforated flaps.

⁵ www.who.int/entity/impact/events/IMPACT-ACTechnologiesv3LIS.pdf

If the structure of the pack is compromised (flaps ripped or unglued, seal broken), it becomes evident to the end user that tampering has occurred prior to consumption, which serves as a way to notify the end user that the product may be sub-standard and/or counterfeit and is therefore at risk. These packaging techniques therefore help to guarantee the integrity of the pack's content. This is in fact already currently widely applicable to many common consumer products such as food packages found in supermarkets.

However, by accepting repackaging practices for pharmaceutical products, current legislation allows the original pack to be discarded or over-boxed by a third party and to be replaced with a new box which does not contain the original pack's anti-counterfeiting features designed to protect and guarantee the integrity of the product incorporated therein. As a result, the patient is no longer assured of the authenticity of the medicine through the security features. Not only is the investment in these features by the manufacturer rendered useless by repackaging activities, but more importantly, it provides an open door for any illegitimate party to infiltrate the legitimate supply chain with potentially dangerous products, by taking advantage of an already opened and therefore unsecured package. In fact, who would buy a pack of breakfast cereal in a supermarket where the perforated seal has been broken and where it is evident that the box has already been opened?

As a result, it has now become essential to ensure that the integrity of original package is absolutely guaranteed throughout the entire supply chain, from the time it leaves the original manufacturers' hands to the point that it reaches the end user. This means that the right to opening the outer packaging should be restricted to the original full marketing authorization holder (i.e. original manufacturer) and the end-user (hospital, health care professional, or patient) **only**, and possibly to parties authorised by the original manufacturer under specific circumstances.

This supposes a ban on repackaging at European level, as proposed in the European Commission consultation paper. There is one important exception to this rule, which is preserving the ability of a duly authorized sponsor of a clinical trial to repackage medicines in accordance with the clinical study protocol. Any legislation will have to make provision to ensure that clinical trials and other research activities are clearly out of scope of any legislation arising out of the Commission's initiative⁶.

EFPIA believes that a risk-based approach may no longer be appropriate to apply these measures, as counterfeiters are now targeting a growing range of medicines and will simply move to target any weaknesses in the supply chain. Additionally non implementation of this policy provision across the full range of pharmaceutical products for human use requiring a prescription might lead to a distortion in competition on cost or convenience of use grounds between drugs with and without a sealed package.

Beside the costs of the tamper evident features burdening only some pharmaceutical companies, a seal would potentially influence the behavior of

⁶ e.g. in clinical trial activities involving the supply and repackaging of "comparator" products and the use of investigational medicinal products; and some instances where the marketing authorisation holder may legitimately wish to repack his product).

some stakeholders involved and generate some discrimination amongst products.

EFPIA therefore believes the measure should apply equally to all prescription medicines. A stepwise approach to its implementation will, however, be necessary, as the application of the technologies across all packaging lines will take time to implement. A risk-based approach should be considered by the manufacturer in selecting priority product while working itself up to full product coverage. However, the selection of which technology to apply on its product should remain the responsibility of the manufacturer who is best positioned to identify which tamper evident feature or combination of features is most appropriate to utilise.

4.1.4. 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.

4.1.5. Mass serialization 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 organisations.

EFPIA position:

EFPIA supports the principle of strengthening records at individual pack level as identified under sections 4.1.5. EFPIA considers that developing a product information interchange system linking both ends of the supply chain, based on uniquely identifiable (i.e. mass serialized) product packs (including batch number information) provides the most adequate level of security while ensuring enhanced patient safety benefits at the point where it reaches the patient (i.e. the pharmacy).

EFPIA would like to stress the complexity of implementing a full-fledged traceability system accessible by all actors in the distribution chain such as a pedigree⁷ (even at batch level only) as proposed in section 4.1.4, which would deliver little added value in terms of patient safety, as opposed to an end-to-end verification system. EFPIA believes that this would constitute a disproportionate measure.

⁷ Pedigree: a document or electronic form containing information that records each distribution of a prescription drug, from sale by manufacturer, through acquisition and sale by any wholesaler or re-packer, until final sale to a pharmacy or other person administering or dispensing the drug.

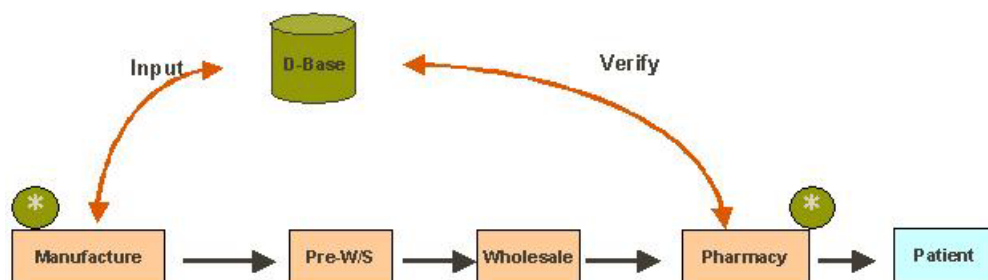
Rationale.

While tamper evident features and the use of authentication technologies present an initial first layer of security, it must be noted that these features can potentially be copied and alone do not constitute an absolute barrier to reduce counterfeits. It has therefore become clear that the development of increasingly sophisticated traceability systems will become in the long term key elements of any comprehensive anti-counterfeiting strategy in Europe.

After an in-depth reflection, EFPIA considers that in order to minimise the risk of substandard or counterfeit products reaching the patient, there is essentially only one point where one really needs to know that the product is safe, that is before it reaches the patient at the final stage of the supply chain (when it is dispensed to the end user at the pharmacy or hospital).

This has led EFPIA to put forward a recommendation to develop a harmonised system for the coding of each pharmaceutical handling unit (individual pack level) based on the Data matrix code (ECC 200) and containing the following information: a product code (identifying the product and its manufacturer), the expiry date of the product, a randomized serial number to enable the unique identification of each unit of sale and the batch number.

EFPIA is also currently developing an end-to-end product verification system allowing a systematic control of each pack's serial numbers at the point of dispensing before it reaches the patient.



By scanning each pack, the pharmacist will be able to check the product 'status' through a web link system accessing a central manufacturer's database (according to an IS architecture to be designed) to verify the authenticity of each dispensing unit before it reaches the patient.

Under the current proposal, product verification is defined as the action of comparing the data held within the product code with a secure product record on a database and confirming that:

- a) The product record exists and matches the data held on the product itself;
- b) The product record has not been previously marked as 'dispensed';
- c) The product record does not contain any warnings or advisory notices (such as recall, on-hold, expired etc).

Product verification does not guarantee the genuine nature of the product contained within the coded product pack. What it does is to provide a mechanism whereby product information such as expiry date and batch codes can be determined, and any duplicate instance of product code (implying an error condition) can be detected prior to widespread proliferation of a potential problem, such as counterfeiting or tampering. The use of the randomly serialised

code generated by a highly secure algorithm simply breaks the business model of the counterfeiters, as there is no 'business' to be made in putting one copy of a unique code on one individual counterfeited pack, which would need to beat the original pack to the pharmacy counter. This concept of checking the product at the point of dispensation also effectively serves to assist the fighting of reimbursement fraud, which is an important issue for many national governments.

The inclusion of the batch number as part of product records in combination with the end to end system (see EFPIA proposal described above), would therefore allow for batch information data to be centrally accessible through the verification web interlink system without the need to manage the complexity of the aggregation process (packaging affiliation management) or having to infer the unique contents of a container.

Therefore, EFPIA considers that enabling batch information to be centrally accessible to all actors in the supply chain is certainly a step in the right direction in order to effectively address the issues of counterfeit or expired medicines as well as to facilitate product recall procedures. It must be noted, however, that the concept of implementing a pedigree system (whether electronic or not) is a highly complex process to implement for all actors of the supply chain and which offers only limited added benefit in terms of ensuring product security and patient safety compared with an end to end system which ensures that only safe products reach the patients.

Indeed, the development of an e-pedigree system is complex because it involves that each manufacturer is able to ensure that the relationship between each pack and other levels of packaging is accounted for. Ensuring a digitally signed tracking information system for each step in the chain requires each actor in the supply chain to have an understanding of the unique contents of each container from the container code via a database enquiry. In order to avoid this, an ePedigree system therefore requires manufacturers to manage the 'affiliation' or 'aggregation' between the different levels of packaging, which allow supply chain partner to have a clear idea of which items, at a unique pack level, they have in their possession. While this is theoretically a straightforward task, it is however fraught with challenges at the level of packaging lines but it is also difficult to handle from a logistical point of view. A more detailed description of the implications of e-Pedigree on packaging lines as well as its effects on the supply chain can be found in [annex 1](#).

EFPIA therefore considers that product 'verification' at point of dispensation for each unit pack via the mass serialisation of all finished product packs provides the most adequate level of security while ensuring enhanced safety benefits at the point where the product reaches the patient (i.e. at the level of the pharmacy).

It also provides the various system stakeholders with increased risk management capabilities that enhance patient safety by increasing the likelihood that the product dispensed is both genuine and appropriate. The end-to end system will also allow stakeholders to manage much more efficiently currently challenging processes such as product recalls. This does not necessitate the development of full e-pedigree capabilities that is costly and difficult to implement.

A harmonized standard

The EFPIA solution relies on product being coded at the pack level in a manner that is common with other products used within the same territory and unique among all products. Ideally the system would employ a common European product-coding standard in order to capture the cross border trade element of the current European supply chain environment.

Indeed, today a majority of European countries use their own coding and identification systems requiring companies to comply with a wide range or requirements. As a result, the integrity of the medicines supply chain is continuing to fracture and opportunities to improve patient safety at a European level and enhance the control of the supply chain are being lost, while the multiplication of systems adds incremental production costs for manufacturing and increases further both the complexity and differentiation across the European market.

EFPIA is currently carrying out a study on the economic benefits of a harmonised coding standard in Europe and the cost associated with no action at the European level (i.e. the development of 27 different coding and traceability system in Europe). This report will be submitted to the European Commission when finalized in the second half of May.

An important element of the EFPIA coding project will be to attempt to harmonise coding systems across Europe. In order to do so, the implementation of unique coding standard for pharmaceutical products identification will be necessary. EFPIA has therefore developed a proposal to harmonise pharmaceutical coding and identification systems in Europe around the existing GS1 open standard⁸ and the use of the Data Matrix code ECC200. EFPIA is currently working with its supply chain partners as part of a steering committee (manufacturers, wholesalers and pharmacists) to develop the operational requirements and work with EU Member States authorities to implement this standard throughout Europe.

A full description of the EFPIA project on coding and identification entitled 'Towards safer medicines supply - A vision for the coding and identification of pharmaceutical products in Europe' can be found in [Annex 2](#).

EFPIA therefore calls for the European Commission to help facilitate the harmonization process by ensuring greater convergence in Member States' initiatives relating to coding and identification systems.

4.1.6. Increasing transparency concerning authorised wholesalers through a Community database

Key ideas for changes to EC legislation submitted for public consultation

- Require GDP certificates to be issued after each inspection of a wholesaler.
- Establish a Community database of wholesalers (including distributing manufacturers) documenting GDP compliance. This could be achieved via extension of the EudraGMP database.

⁸ <http://www.gs1.org/>

EFPIA position:

There should be a system established following the lines of ISO certification. The WHO/IMPACT GDPs might serve as a content basis.

The idea to extend the existing EUDRA GMP database with GDP certificate owners should be supported. However, EFPIA would recommend that sufficient consideration be given to managing data protection issues with the sharing of such records. If the record was accessed inappropriately, this may assist criminals in identifying which warehouses to target for various illegal activities.

Section 4.2. Tightening requirements for the import/export/transit (transshipment) of medicinal products

Key ideas for changes to EC legislation submitted for public consultation

Directive 2001/83/EC would be clarified to the effect that imported medicinal products intended for export (i.e. not necessarily subject to marketing authorisation) are subject to the rules for imports of medicinal products. The following provisions would apply:

- The obligatory importation authorisation under the conditions set out under Article 41 Directive 2001/83/EC, e.g. relating to premises and the qualified person;
- the relevant obligations for the importation authorisation holders set out under Articles 46 and 48 Directive 2001/83/EC, e.g. relating to staff and access for inspection;
- the obligations stemming from Article 51(1)(b) and (2) Directive 2001/83/EC, relating to qualitative and quantitative analysis of the imported medicinal product; and
- the relevant obligations stemming from Directive 2003/94/EC on good manufacturing practice.

The corresponding rules on inspections would apply.

EFPIA Position:

EFPIA fully support that goods in transit and for export should be subject to the rules for imports of medicinal products

Rationale

- It is necessary to clarify that shipment into one of the EU Member States for transit purpose is sufficient to apply the EU laws /regulations on IP rights and counterfeiting.
- However, there should be some provision to waive the need for full and routine analysis (importation re-testing) of imported product where there is clear evidence that systems are in place to demonstrate the quality and integrity of the product being exported. Re-testing adds little assurance when a robust pharmaceutical quality system is in place. Inspections and testing by the customs authorities should be possible in case of suspected counterfeit goods, whether the goods are destined for the market or not, based on the principle of proportionality.
- It would be helpful if the Directive would, in an Article (not in a Whereas clause), comprise a definition of important terms that affect the legal interpretation and use of the Directive, such as “import”, “export”, “counterfeit”⁹, “transshipment”, and “transit”.
- The WHO/IMPACT document entitled “Principles and Elements for National Legislation to Combat Counterfeit Medical Products” was endorsed by the General Meeting on 12/12/07 in Lisbon. In this project, IMPACT defined specific obligations and responsibilities to address the so-called problem of “double standards” for medicines for the local market and for export. The

⁹ We recommend defining a counterfeit as per the WHO definition.

document is meant to give guidance to governments and parliaments for the establishment of national legislation. EFPIA fully supports this project, partly funded by the European Commission (under the Competitiveness and Innovation Framework Programme), and which it should take into account in its strategy on counterfeit medicinal products.

4.3. Tightening requirements for manufacture, placing on the market of active substances and inspections

4.3.1. Requirement of a mandatory notification procedure for manufacturers/importers of active substances

Key ideas for changes to EC legislation submitted for public consultation

Submit the manufacturing/import of active ingredients to a mandatory notification procedure.

Render information on notified parties available in a Community database. This could be achieved via extension of the EudraGMP database.

EFPIA Position and rationale:

As unknown impurities coming from unknown manufacturing processes represent the highest risk on safety for the patient, the most relevant information is whether the API has been manufactured according to the registered manufacturing process with the registered impurity profile.

Accountabilities and roles and responsibilities for any API notification procedure need to be clearly defined for the different “actors” in the supply chain. Minimum qualifications and experience for “qualified auditors” for API should be specified.

In order to focus resources effectively, a risk-based approach is necessary and cooperation with and acceptance of inspection reports from other agencies should be sought to minimise duplication of existing regulatory requirements, which are already part of product authorisation submissions.

4.3.2. Enhancing audit and enforceability of GMP

Key ideas for changes to EC legislation submitted for public consultation

- Make regular audits of active substance suppliers on GMP compliance by manufacturers and importers of medicinal products mandatory. Auditors should be sufficiently qualified.
- Require, where scientifically feasible, control of active substances via sufficiently discriminating analytical techniques, such as fingerprint technologies, Near Infrared Spectroscopy (NIR), as a mandatory method for identification by the manufacturer of the medicinal product. Such a testing is meant to identify deviations of the manufacturing process and manufacturing site for each batch.
- Turn principles of good manufacturing practice for active substances placed on the Community market into a legal act of Community law (e.g. a Commission Directive) in order to enhance enforceability.

EFPIA Position and rationale:

- It is not clear how more GMP audits would contribute to enhancing product safety. GMP standards already give pharmaceutical manufacturers the duty of ensuring the quality of supplies by establishing adequate supplier management and controls. The key question is whether the manufacturing process has followed the registered manufacturing process – a question of regulatory compliance more than a GMP question.
- Minimum qualifications and experience for “qualified auditors” for API should be specified.
- Every delivery of an API should undergo a testing of unknown impurities using fingerprint technologies. However the cost implications of introducing Near Infrared Spectroscopy (NIR) tests for all APIs needs further review. It must be noted, however, that imposing this type of testing could risk promoting reliance on receipt testing which is no substitute for good supplier management based on a risk assessment, technical agreements, change control, knowledge of products, process performance, etc.
- There is variability as to which Member States do routine API inspections and those who do not. Cooperation with and acceptance of inspection reports from other agencies should be sought to minimize duplication.

4.3.3. Enhancing GMP inspections

Key ideas for changes to EC legislation submitted for public consultation

The competent authority may carry out announced or unannounced inspections of active substance manufacturers in order to verify compliance with the principles of good manufacturing practice for active substances placed on the Community market.

The competent authority shall carry out these inspections if there is suspected non-compliance with GMP.

The competent authority shall carry out repeated inspections in the exporting country if the third country applies standards of good manufacturing practice not at least equivalent to those laid down by the Community or if mechanisms for supervision and inspections are not at least equivalent to those applied in the Community. To this end, a Member State, the Commission or the Agency shall require a manufacturer established in a third country to undergo an inspection.

EFPIA Position:

EFPIA supports the proposed key ideas listed under section 4.3.3

Rationale:

Counterfeits may be found following the detection of unknown impurities. Laboratories (such as EDQM) could check this. They could use fingerprint

technologies to analyze the APIs. It could also be done by independent quality laboratories.

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