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Contribution from Groupement des Pharmaciens de L'Industrie en Europe (European Industrial Pharmacists' Group), to the Public Consultation in Preparation of a legal proposal to combat Counterfeit Medicines for Human Use

Introduction

The European Industrial Pharmacists Group concurs fully with the concerns of the European Commission regarding the increasing counterfeiting activity in the field of medicinal products. The European Industrial Pharmacists Group is in agreement with most of the proposals forwarded by the Commission, particularly those relating to the tightening of requirements for the import/export/transit (transshipment) of medicinal products, and feels that these measures would indeed be effective in decrease counterfeit medicinal product penetration into the European Union. Following internal discussion amongst its members, the EIPG wishes to offer the following comments concerning proposals made in the EU Consultation Document.

1. Licensing of brokers, traders and agents

EIPG is in agreement with the Commission's proposal that brokers, traders and agents should be considered as wholesalers, and hence subject to the respective legal obligations. Indeed, it would not be amiss to take the position that all actors in the distribution chain should be either holders of a manufacturing authorization[1] - and hence distributing the manufactured products by virtue of said authorisation[2] - or holders of an authorisation to engage in activity as a wholesaler[3]. In the latter case, this requirement should be enforced irrespective of whether the actor physically distributes the product as part of the activities or is merely acting as a broker, trader or agent. Failure to do so has the potential to result in problems at the wholesale dealing level downstream of the broker, trader or agent, particularly when the authorized wholesaler needs to rely on the broker, trader or agent for the maintenance of a quality documentation system consonant with principles of good distribution practice, especially in matters relating to regulatory affairs.

Another issue of particular concern is that of on-line trade in pharmaceutical medicinal products, other than through registered internet pharmacies. The problem is particularly acute in Member States either when individuals do not find medicinal products authorized in the Member State or the market prices are high, and revert to obtaining directly the medicine for personal use over the internet, thus obtaining medicine which may be counterfeited.[4] It is readily discernible that all efforts to stem entry of counterfeit medicinal products into the European Union will prove futile unless legislation to ban this method of obtaining medicinal products is implemented in all Member States.

2. Responsibilities

[1] Art. 40 Directive 2001/83/EC.
[2] Art. 77(3) Directive 2001/83/EC
[3] Art. 77(1) Directive 2001/83/EC
[4] Availability of Human Medicinal Products, Report of Task Force of HMA MG, 2007

Audit responsibility is more complex than is indicated in the Commission document .Whilst the Qualified Person is responsible for ensuring the quality, safety and efficacy of every batch of medicinal product released within the European Union, the marketing authorization holder remains the "owner" of the product. Consequently a variety of scenarios may exist with respect to audit responsibilities between manufacturers, wholesale dealers and brokers, traders or agents. The EIPG believes that it would be appropriate for possible scenarios to be outlined, together with appropriate guidance, in a document similar to Annex 16 (*Certification by a Qualified Person and Batch Release*) to Volume 4 (*Good Manufacturing Practices*) of EudraLex: The Rules Governing Medicinal Products in the European Union, rather than attempting to make provisions for all such restrictions within the Directive.

EIPG also believes that the lack of stipulation of qualification requirements, responsibilities and professional accountability for the qualified person designated as responsible[5] for wholesale dealing activities, is a major shortcoming of the Directive. Most Member States are well placed in this regard, having local legislation that establishes that such a person must be a pharmacist, stipulates the knowledge required of such a person, and provides for professional regulation of such persons. However, this is not the case for all EU Member States. A recent recommendation by EIPG has in fact called for an amendment of the Directive in this regard.

Furthermore, EIPG also believes that the current guidelines on Good Distribution Practice (GDP) issued by the Community[6] are somewhat outdated and do not provide sufficient guidance to wholesale dealers, whose GDP activities, particularly where documentation requirements and validation procedures are concerned, are becoming more akin to those observed in Good Manufacturing Practices. More detailed guidelines, similar to those found in Volume 4 (*Good Manufacturing Practices*) of EudraLex: The Rules Governing Medicinal Products in the European Union are recommended. The WHO has recently published its own guidelines for Good Distribution Practices for Pharmaceutical Products, which should form the basis for a similar document issued by the Commission[7].

3. Repackaging

The EIPG agrees that a ban on repackaging, together with the use of security features which are placed on the product by the manufacturer and can only be removed by the end-user, represents a concrete step towards reducing the penetration of counterfeit medicinal products into the European Union.
However, most pharmaceutical manufacturers operate on a minimum order quantity principle, where the sizes of such minimum orders frequently exceed the annual consumption of small-sized markets. This may lead to problems, particularly in countries where specific requirements exist in terms of the language of the packaging and patient information leaflet, and/or the addition of the authorisation number. The EIPG is aware that a ban on repackaging, coupled with economies of scale, will probably drive marketing authorisation holders either to increase their supply prices to cater for small orders, or to withdraw their products from the market. Such actions are quite likely to have a negative impact on the availability and accessibility of medicines in small Member States, thereby potentially compromising public health.

Provided that there is a technical agreement in place between the Marketing Authorisation holder and the local packaging contractor, the EIPG considers that a marketing authorization holder may

[5] Art. 79(b) Directive 2001/83/EC
[6] Commission Guidelines 94/C 63/03
[7] Annex 5, 40th Report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations, WHO Technical Report Series 937, 2006

subcontract repackaging of the product in question. The repackaging operations must not compromise the integrity of the primary packaging and must be carried out under strict compliance with the principles of Good Manufacturing Practices in duly authorized pharmaceutical premises[8]. Furthermore, the finished product must comply with mass serialization and security features incorporated into the Marketing Authorisation holder's product packaging. Good practice principles must be implemented such as processes of secure disposal of the original carton or patient leaflets, to the same level and standards applied when medicinal products are disposed of, thus reducing the risk of counterfeit penetration associated with repackaging operations.

4. Harmonised Databases

The concept of centrally accessible database records is indeed an attractive one, particularly with regards to the extension of the EudraGMP database to cover wholesale dealers. However, with regards to the database of the medicinal products there are at least two concerns that need to be addressed.

a. establishing and monitoring a database requires funds. If these funds are acquired in the form of fees for marketing authorization holders, such increased costs may have a negative impact on to small-to-medium enterprises
b. the further away one moves from the manufacturing source, the more one will have to rely on reliable reporting of product movement by wholesale dealers. Some wholesale dealers will be suppliers of parallel importers or distributors and/or, in a more recent development, suppliers of applicants for Article 126a authorisations[9]. The reliability of data supplied by such wholesale dealers may therefore be questionable as they will not wish to have their activities exposed.

Mass serialization is a key to the authentication process which will allow end-users to ensure that a particular unit serial number has been released by a Qualified Person in the European Union, and agrees with the information present on the outer packaging. The end-users should be restricted to Qualified Persons, Responsible Persons and health care professionals in order to prevent leakage of these mass serial numbers to the counterfeit industry. Several Member States have already introduced European authentication systems and these can be added to pharmacy software to give a range of benefits such as product recalls and alerts for out of date stock. The EIPG also feels that a move towards more widespread use of electronic patient medication record databases should be encouraged.

EIPG feels that the concept of a "lifetime database" is applicable to pharmaceutical manufacturing and analytical equipment, and any essential parts thereof. Second-hand, ex-demo and decommissioned equipment is frequently sold by second-hand vendors and consequently available to counterfeit manufacturers. However, this risk should not preclude the possibility of such equipment being donated to *bona fide* research institutes such as universities. The use of such a database, in combination with the EudraGMP database, would serve to ensure that every piece of equipment has a dossier associated with it, throughout its useful life thus ensuring legal tracing of the equipment together with buyer certification.

8 Art. 40 Directive 2001/83/EC.
9 Art. 126a, Directive 2001/83/EC

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