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Directorate General Enterprise and
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Key Ideas for Better Protection of Patients against the Risk of Counterfeit Medicines

On March 11, 2008, the European Commission published a document entitled "Key Ideas for Better Protection of Patients against the Risk of Counterfeit Medicines" for consultation. First of all, we would like to express our gratitude for having been offered the opportunity to contribute to the development to the future preparation of a legal proposal to combat counterfeit medicines for human use.

As regards the document itself, we would like to share the following comments with you:

We very much appreciate the Commission's initiative to prepare such a legal proposal and feel that a number of important issues have already been identified. However, we feel that there is a need for additional action.

Key ideas 4.1.1. a) Clarify that the obligation for wholesalers apply to all parties in the distribution chain, except for those directly distribution or administering to the patient. Brokers, traders and agents would be considered as wholesalers, with the respective obligations stemming from the pharmaceutical legislation.

Comment: Current GDP-requirements cover adequate storage, separation issues and recalls. However, activities related to procurement of products, which are critical in the context of combating counterfeits, are not regulated. Establishment of GDP requirements on procurement based on sound knowledge of the current practices of pharmaceutical wholesalers, brokers, agents, im- and exporters, could contribute significantly to the minimisation of the risk of an unintended introduction of counterfeited products into the legal distribution chain. The content of such modified GDP-requirements should, as far as applicable, also be relevant for pharmacies and others involved in the dispensation to patients..

Key ideas 4.1.1.b)
Make regular audits of GMP/GDP compliance mandatory by qualified auditors

- of (contract) manufacturers
- between suppliers (wholesalers, manufacturers) at least in cases of suspicion of non- compliance with GMP and/or GDP

Comment: GMP/GDP audits are useful and necessary to assure that a (contract) manufacturer is generally able to manufacture the respective product and has a quality system in place. These audits must be performed by qualified personal and should ideally by performed by independent, accredited and specialized organisations including inspection companies.

Audits are part of the overall package of measures to assure compliance of the legal market for medicinal products. However, it has to be acknowledged that counterfeiters and other criminals do not feel bound by this system and therefore these tools alone cannot be effective to detect or prevent counterfeiting.

Audits of distributors can only be useful if there is a clear regulation of the distribution chain in place, i.e. there is a need for clear guidance/regulation against which inspections/audits have to be carried out.

Key ideas 4.1.3

- 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, ie.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)

Comment: Repackaging is usually a manufacturing step as any other step. Repackaged medicinal products could also be sealed by the manufacturer who performs the repackaging. Proper repackaging does not affect the risk of counterfeits.

Now, sealing can be useful to demonstrate the end users that the package has not been tampered, but is useless to prevent counterfeiting. Unfortunately, also sealings can be falsified as is the case for the whole product. Thus, they can even give the misleading impression to doctors and patients that a sealed product is authentic. In order to provide real confidence and reassurance to end-users, they should be able to check whether a seal is authentic or falsified. Taking into

consideration that average end-users are not even able to recognise counterfeit money, how should they be able to judge authenticity of a seal.

Key ideas 4.1.4
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.

Comment: Tracing on a batch level only is not suitable to detect counterfeits. A batch, usually consisting of thousands of units, is normally distributed to different wholesalers, pharmacies and end users. At any of the different distribution stages, part of the original batch can be replaced or enlarged by counterfeits with the same batch number, which would not necessarily be noticed with such a system.

Key ideas 4.1.5
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.

Comment: Authentication of each single unit of a medicinal product is the only effective approach. Nevertheless, authentication only on the regular distribution chain is not sufficient to reassure and protect patients. It is mandatory that the patient has the possibility to check authenticity of a product, regardless of how he received the product. However, it is not sufficient to restrict these measures to the legal distribution chain as products may unknowingly be purchased from illegal sources. Therefore, it is vital to provide the end-users with tools to check whether the product in their hand is authentic. A counterfeit product can reach the end-user by total avoidance of the legal distribution chain.

Key ideas 4.1.6
- 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.

Comment: Establishment of a community database of ALL actors in the supply chain (manufacturers, importers, wholesalers, pharmacies) could help to identify whether a product has been supplied from the legal distribution chain or not.

Key ideas 4.3.3
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 on 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.

Comment: Imports of medicinal products and APIs from countries with inequivalent to the EU GMP requirements and regulatory control mechanisms should be principally excluded. In exceptional cases, manufacturers who voluntarily subject themselves to the application of the relevant EU standards and who legally commit themselves to pay penalties for any violation of these rules should be allowed to import their products into the EU. Prerequisite for such an exception should be a sound GMP inspection, carried out by an accredited EU inspection body, allowing only a limited number of minor and no major findings. In addition, the manufacturer should commit to elaborate an action plan for the continual improvement of their compliance and to regularly report the progress to the relevant GMP inspection body. In case of deviation from the action plan, legal measures should be established to immediately stop distribution of medicinal products containing substances from this specific non-compliant source. In addition, it should be considered to introduce the requirement of a successful GMP inspection or audit by an accredited inspection body before APIs from a given source may be accepted for the first time in a marketing authorisation procedure.

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