ROCHE RESPONSE TO THE EUROPEAN COMMISSION PUBLIC CONSULTATION IN PREPARATION OF A LEGAL PROPOSAL TO COMBAT COUNTERFEIT MEDICINES FOR HUMAN USE

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I. GENERAL REMARKS

Roche welcomes the European Commission's public consultation in preparation of a legal proposal to combat counterfeit medicines for human use as an important opportunity to share its views on this topic. First and foremost, Roche wants to express its full support to the contribution made by the European Federation of Pharmaceutical Industries and Associations (EFPIA) to the consultation. EFPIA's views and concerns on the matter expressed in its response reflect the convictions held by Roche on a new legislative framework to improve combating counterfeit medicines for human use. Nevertheless, Roche would like to take the chance to highlight some specific aspects and express some supplementary thoughts.

Counterfeiting of pharmaceutical and diagnostic products constitutes a significant public health issue worldwide. It is an increasingly common crime that, in addition to infringing intellectual property rights:

– endangers the lives and the well-being of patients;
– undermines confidence in healthcare systems and health professionals;
– creates a financial burden on patients and governments because of the money wasted on counterfeits and related enforcement measures;
– damages public confidence in authentic pharmaceutical and diagnostic products and their manufacturers and distributors, adversely affecting these legitimate businesses.

Roche fully supports the fight against counterfeit pharmaceutical and diagnostic products with the primary objective of protecting patient safety and health and therefore welcomes the recent EU initiatives in this area. Roche also agrees with the plan to implement mechanisms for tracing and authenticating pharmaceutical and diagnostic products from the manufacturing to the dispensing level.

From an industry point of view it is of utmost importance to avoid fragmentation of traceability systems. The coexistence of different technologies will not only increase production costs but also require different reading devices and databases and corresponding administrative structures. All stakeholders in the supply chain have to participate to the same system in order to effectively address the network dimension of the counterfeiting challenge.

The proposed set of key ideas should be considered as part of a comprehensive strategy focused on ensuring that only the safest products reach the patient but also by strengthening the integrity of the supply chain:

Making the product safer

– Using tamper-evident packaging and labelling on all products
– Using overt and covert authentication features
– Strengthening product identification at individual pack level through a harmonised coding standard

Strengthening the integrity of the supply chain
– Introducing a ban on repackaging
– Reducing the number of actors in the supply chain
– Auditing of the supply chain by authorities
– Clarifying the liability of parallel distributors
– Notifying of corrupt products

Complementary measures
To combat counterfeiting of pharmaceutical and diagnostic products, it is necessary to address the different aspects of this serious criminal activity.
We would like to take this opportunity to urge the Commission to take flanking measures to address the counterfeit pharmaceutical and diagnostic products 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 pharmaceutical and diagnostic products. We 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 pharmaceutical and diagnostic products. Criminal penalties are particularly important in the medicines' sector due to the foreseeable harm caused to human health and safety.
– Tackling sales of counterfeits over the internet
  The sale of counterfeit pharmaceutical and diagnostic products over the internet is a critical and growing problem in Europe, which needs to be addressed. We believe that both public health authorities and pharmaceutical companies have an important role to play in educating consumers on the risks posed by counterfeit pharmaceutical and diagnostic products offered via the Internet.
– Proper law enforcement
  The proposed controls will require proper law enforcement. 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.
– International enforcement
  Treaties for international enforcement of judgments are also desirable to prevent criminals from moving from one country to another. We would like the Commission to consider how it could use influence to support countries outside of the EU where counterfeit pharmaceutical and diagnostic products may originate to minimise the impact of this illegal activity. We realise that the responsibility for the various elements mentioned here lie with different DGs in the Commission so that inter-DG cooperation and exchange of information is absolutely key.

II. SPECIFIC COMMENTS ON THE COMMISSION'S CONSULTATION PAPER[1]

4. KEY IDEAS FOR BETTER PROTECTION OF PATIENTS AGAINST COUNTERFEIT MEDICINES

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

a) 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.

Roche position and rationale:
Roche fully supports the proposed key ideas listed under section 4.1.1.

Any supply chain control has to be audited to ensure that the implemented measures are working in the desired way. Traders, brokers and agents are not currently inspected and audited.
There should be a legal framework for extending GMP auditing system by including auditing the supply chain. In this respect, we are supportive of the need for a harmonized EU framework to avoid different approaches by national agencies and ensure predictability of operations for global healthcare industry.
To ensure wholesalers and 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.
The minimum qualifications and experience for "qualified auditors" should be defined. We recommend that health authorities should conduct these audits. 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

[1] Numbering refers to paragraphs in the Commission's consultation document

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.
Manufacturers need to work together with the authorities, as in GMP, because companies cannot do the audits alone. We strongly recommend that health authorities should conduct these audits. National health agencies should be entitled to perform "safety audits" along the whole supply chain from manufacturer to the point of dispensing and customs should be included in the regular safety audit plan of the supply chain. Traders and brokers cannot inspect each other because they are not experienced to do so.
In the new business model where the parallel trader distributes blister 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).

Roche position and rationale:
Roche supports the proposed key ideas listed under section 4.1.2.

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 that wholesalers 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.
Although in principle we are supportive of tighter governance procedures for inspections in third countries, experience 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 dissimulate 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 audits.

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).

Roche position and rationale:
Roche supports the proposed key ideas listed under section 4.1.3. However, we believe 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. We believe 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.

Roche believes that the number one focus of the legislative reform should be 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.

However, by accepting repackaging practices for pharmaceutical products, current legislation allows the original pack to be discarded 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 the integrity of the product incorporated therein. 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 eventually to parties authorised by the original manufacturer. This supposes a ban on repackaging at European level, as proposed by the European Commission.

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 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 organisations.

Roche position and rationale:
Roche supports the principle of strengthening records at individual pack level as identified under sections 4.1.5. Roche believes this is best achieved by implementing an end to end product verification system of each individual unit at the point of dispensation rather than a full track and trace system such as a pedigree.

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.
The research-based pharmaceutical industry having reflected on this issue, considers that in order to guarantee product security throughout the supply chain, there are essentially only two points where one needs to know that the product is safe, that is, when it goes into the supply chain and when it reaches the final stage of the supply chain.
This has led EFPIA to put forward a recommendation, supported also by Roche, 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.
A more detailed description can be found in the EFPIA Response to the Public Consultation in preparation of a legal proposal to combat counterfeit medicines for human use in section 4.1.5.

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.

Roche position and rationale:
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. But we 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.

4.2. Tightening requirements for the import/export/transit (transhipment) 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.

Roche position and rationale:
Roche fully supports that goods in transit and for export should be subject to the rules for imports of medical products.

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. This should comprise the rules against infringement of trademark rights. Under present law, the trademark owner is not entitled to invoke his rights against counterfeits in transit (see ECJ C-405/03). To close this loophole is of outmost importance.
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.

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.

Roche 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.

Roche 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. Minimum qualifications and experience for "qualified auditors" for API should be specified. We strongly recommend that health authorities should conduct these audits at least in cases of non-compliance with GMP and/or GDP.
Where scientifically feasible, control of active substances via current technologies should be assessed for suitability in order to identify the manufacturer of the medicinal product. 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.

Roche position and rationale:
Roche supports the proposed key ideas listed under section 4.3.3