Johnson & Johnson

Johnson & Johnson response:

EUROPEAN'S 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

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Introduction

As the world's most comprehensive and broadly based manufacturer of health care products, as well as a provider of related services for the consumer, nutritional, pharmaceutical, medical d evices and diagnostics markets, Johnson & Johnson is fully committed to playing its part in shaping the healthcare environment.

Johnson & Johnson has approximately 119,200 employees worldwide engaged in the research and development, manufacture and sales of broad range of products in the health care field. Our company conducts business in virtually all countries of the world and had sales of $ 61.1 billion for 2007 with the primary focus on products related to human health and well -being.[1]

Caring for the world . . . one person at a time ™ inspires and unites the people of Johnson & Johnson. We embrace research and science - bringing innovative ideas, products and services to advance the health and well-being of people. Employees of the Johnson & Johnson Family of Companies work with par tners in health care to touch the lives of over a billion people every day, throughout the world.

General Comments

Johnson & Johnson believes that healthcare issues should be approached in a holistic way. Activities in the area of public health should no t only focus on health promotion and disease prevention, they should also take account of the care, treatment and services provided to patients. These measures should be of benefit and of high quality. In this respect, Johnson & Johnson supports the aim of the EU Commission to amend the legal framework for medicinal products in its effort to combat the counterfeiting of medicinal products.

Counterfeit medicines reach patients faster than ever, in dramatic proportions, as showcased within the *"Summary of community customs activities on counterfeit and piracy"* , 2006 [2], where medicinal products are on the 6th place amongst all commodities seized by EU Customs.

Counterfeit medicines have become the single most important threat to patients' safety. The trends presented within the EU Commission Consultation report do not only reflect the current situation, but also indicate a frightening tendency of counterfeiters towards dealing in life saving medicines, using ruthless practices.

It should be clear and stres sed that any single case of counterfeit medicinal products seized by EU customs, could potentially represent thousands of undetected products that could reach the EU's citizens and patients. Therefore we applaud the EU Commission report of medicinal produc ts seized by EU customs during 2006, as it presents in absolute numbers the issue in its proper perspective.

We welcome the invitation to participate in the Commission Consultation as a significant start in addressing the key elements of the counterfe it issue; nevertheless, we maintain that more actions are needed to fully tackle the issue effectively within the EU.

Specific responses to the Consultation's key ideas for better protection of patients safety against counterfeit medicines

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

[1] 2007 Annual Report: http://www.jnj.com/our_company/annual_report_videos/index.htm

[2] European Commission, Taxation and Customs Union. (2007)

Summary of community customs activities on counterfeit and piracy . Available at:

http://ec.europa.eu/taxation_customs/resources/documents/customs/customs_controls/counterfeit_piracy/ statistics/count erf_comm_2006_en.pdf (Date accessed: 11/04/08)

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

Johnson & Johnson welcome's the Commission's intention for clarifying " *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."*

However, we believe that the Commission should also focus on facilitating, promoting and encouraging a more 'direct' supply of medicines from manufacturers to patients, it being understood that manufacturers will continue to work with legitimate intermediaries where necessary. Regardless of the legislative framework, if the supply chain continues to be as complex, counterfeiters will identify different entry points each time. The result will be a fragmented and unsecured supply chain that will not only increase the time of distribution and provide opportunities for storage and handling errors but will also make counterfeiting practices invisible to inspections.

Furthermore, we suggest that the Commission should clarify by naming who is excepted from the above proposed obligations. Hence, the Commission should clarify what is meant by " *those directly distributing or administrating medicinal products to the patient* ". We believe that the forthcoming legislative framework should diminish every potential "window" for actors in the distribution chain to escape from their legal obligations.

We support the key idea of " *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".*

We believe that the WHO/IMPACT *"Draft Principles and Elements for National Legislation against Counterfeit Medicinal Products"* could be used as an archetype for EU and national legislative provisions aiming to make all actors of the supply chain accountable. Furthermore, we urge the Commission to strengthen the penalties in cases of corrupt practices and that even negligence be considered as a criminal act.

4.1.2. Tightening rules on inspections

Johnson & Johnson supports the proposed key idea to " *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"* and we also support *"the inclusion of specific harmonised provisions for inspections by competent authorities of parties in the distribution chain (e.g. wholesalers, brokers, traders, agents, business-to-business platforms)"*

We welcome the Commission's suggestion to inspect traders, brokers and agents as this is not the current situation. In addition, we consider that the inspection procedures should be used as a blueprint for national agencies to ensure a harmonized system in the EU. Indeed, if the inspection procedures are harmonized taking into account national differences then best practices could be shared and the system will be stronger against practices that aim to manipulate 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

Johnson & Johnson does not support the key idea, which " *requires the outer packaging of medicinal products to be sealed. This would reveal any subsequent opening of the packs".*

We propose the adoption of tamper evident packaging accompanied by the development and adoption of a full track and trace system.

Furthermore, as the Commission accurately identified within the Consultation paper, there is a misuse of original packs after repackaging and counterfeiters target specific sources within a highly complex

distribution chain. Thus, a requirement for tamper evident packaging should be introduced along with an immediate ban on repackaging by all actors in the distribution chain. Repackaging should only be permitted by, or under the control of, the Marketing Authorisation holder or the Marketing Authorisation holder's designee under appropriate circumstances.

Furthermore, Johnson & Johnson remains skeptical regarding the notion that " *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."*

As patients' safety is our first concern and obligation, according to our Credo[3], we do not support a risk-based approach. As it was identified by the Consultation paper, counterfeiters target life-style and life-saving products, thus, we principally believe that the only way to avoid fatal consequences to patients lives is to adopt a tamper evident feature to all prescribed medicinal products. However, significant time should be granted to make the many operational and information systems changes that are needed to revise packaging components and equipment.

Regarding *"the right to opening the outer packaging would be restricted to the market authorisation holder and end-user (hospital, health care professional, or patient)"* we believe that there should be a specific process of book-keeping of all packages opened by specific categories of end users (hospitals) as we would not like to witness a shift of counterfeiters target from repackagers to end-users.

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

Johnson & Johnson supports the key idea " *requiring the possibility of tracing ownership and transactions of a specific batch. This should be achieved by making a specific record (pedigree) obligatory."*

With respect to our points raised in 4.1.1 and 4.1.3, we firstly maintain that the Commission should consider facilitating, promoting and encouraging the direct distribution of medicinal products by manufacturers to the extent that it is practical. Also, the Commission should firmly legislate the ban of repackaging by all except the Marketing Authorisation holder or the Marketing Authorisation holder's designee. We believe that the former will add value in simplifying the supply chain and thus the traceability of medicinal products and that the latter will make the key idea possible, since repackaging would ultimately cancel any obligatory pedigree and authentication markers on the outer packaging unless repackaged under the control of the Marketing Authorisation holder using the same methods of pedigree and authentication markers.

On the concept that " *the record should be accessible by all actors in the distribution chain"* we believe that the Commission's key idea neglects basic competition and market share information exclusivity rules and thus we cannot support such a suggestion.

To address the need for a centralized pedigree, we suggest that different actors in the distribution channel should have different levels of accessibility:

- Competent Authorities should have access to all records and distribution paths for all medicinal products;
- Marketing Authorisation holders should have access to their products path, from manufacturing up to the last traceable point;
- All other actors (wholesalers, pharmacies/retailers) should have access only to the information pertaining their respective source of product (*i.e.*, to the previous point of distribution) and not the whole record.

The above distinctions will enable Competent Authorities to monitor the distribution channels as well as the process of product recalls by manufacturers, when such measure is required and, in addition, respects the confidential information of volumes sold to specific sources/markets.

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

[3] Johnson & Johnson CREDO:
http://www.jnj.com/our_company/our_credo/index.htm

Johnson & Johnson supports the key idea *"requiring 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."* We believe that mass serialization features incorporated in the "selling" pack will enhance the traceability efforts and the monitoring of the supply chain.

On the issue of the categories of products that will require such serialization features, as we noted in the 4.1.3 section, we believe that serialization characteristic should be implemented to all prescribed medicinal products.

Nevertheless, we recognize the need for cost-efficient and cost-effective solutions that will be feasible for all the 2,200 pharmaceutical companies [4] represented in Europe since many of them are SME. Having stressed that, we suggest the mass serialization features to be implemented to medicinal products in three phases:

1. Widely counterfeited medicinal products (according to WHO lists and EU Customs seized products);
2. Life saving medicinal products;
3. All prescribed medicinal products.

Given that the industry is already engaged in the area of mass serialization through EFPIA's project on Coding & Identification, we suggest that the EU Commission to explore the possibility of liaising with EFPIA in this project in order to avoid any duplication of similar work. Such cooperation will facilitate the EU Commission's endeavors in clarifying the technical details within the implementation of the legislative initiative. In looking beyond the borders of the EU, many countries are also implementing similar requirements under a variety of coding structures and standards. It is important to the industry as a whole to devote attention to the best regional and global standards for mass track & trace serialization solutions.

4.1.6. Increasing transparency concerning authorized wholesalers through a Community database

Johnson & Johnson fully supports the key idea "*for 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."*

We maintain that all actors in the supply chain should be subject to appropriate GMP/GDP rules and that there should be a list documenting compliance and certification. The EudraGMP database is a visible solution that we support. However, we would recommend that sufficient consideration be given to managing Data Protection issues with the sharing of such records.

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

Johnson & Johnson principally supports the key ideas for EU legislation changes:
"*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."

We believe that the aforementioned legislative changes will assist the EU Commission's endeavors in eliminating all possible entry points for counterfeiters and that they are aligned with the WHO IMPACT's proposals to address "double-standards" for medicines for local markets and export.

[4] EFPIA's data : http://www.efpia.org/content/Default.asp?PageID=349

However, there should be some provision to waive the need for some requirements based on an assessment of the controls and agreements in place between the actors of the import/export/transit chain, in particular in cases where these transactions are occurring within the same company and are being govern ed by the same quality management system. For example, the need for full and routine analysis (importation re - testing) of imported product is seriously questioned where there is evidence that systems are in place to demonstrate the quality and integrity of the product being exported; retesting adds little assurance when a robust pharmaceutical quality system is in place.

In addition, we believe that all actions aiming to strengthen the EU Commission's ability to identify and seize counterfeit medicinal pr oducts could be assisted by further cooperation with law enforcement agencies, Customs, as well as postal authorities. The latter will help the Commission to address the issue of counterfeited medicines commercialized through illegal Internet pharmacies.

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

Johnson & Johnson fully supports the ke y idea by the EU Commission to *"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 data base."* However, in order to limit the administrative burden for both regulators and pharmaceutical companies, care should be exercised so as not to duplicate submission of information that is already part of other regulatory processes such as Marketing Aut horisation applications.

As counterfeited active ingredient can pose significant risk for patients' safety, we maintain that the EU Commission's suggestion adequately addresses the issue and we strongly believe that all players of the manufacturing proces s should comply.

4.3.2. Enhancing audit and enforceability of GMP

Johnson & Johnson supports the key idea for *"regular audits of active substance suppliers on GMP compliance by manufacturers and importers of medicinal products mandatory. Auditors should be sufficiently qualified.*

However, we believe that the key idea to *"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.",* should be carefully evaluated. Assuring the purity of active ingredients is extremely important to protect the patients' safety. However, it is generally accepted that end product testing is not a substitute for good process control and supplier management based on, for example, risk assessment, tec hnical agreements, change control, product and process knowledge, process performance. Furthermore, imposing this type of testing could risk promoting reliance on receipt testing only, being contradictory to all principles of good quality management, and t hus provide a fall sense of security.

In addition, we do not support the key legislative idea to " *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"* since such legislative provision will add more regulations to an already fragmented industry and will append bureaucratic procedures in cases of updates or changes needed.

4.3.3. Enhancing GMP inspections

Johnson & Johnson principally supports the key idea of *"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 substanc es placed on the Community market. The competent*

authority shall carry out these inspections if there is suspected noncompliance with GMP. The competent authority shall carry out repeated inspections in the exporting country if the third country applies st andards 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 o r the Agency shall require a manufacturer established in a third country to undergo an inspection."

We maintain the notion that official inspections are crucial for effective enforcement. In this respect, the EU Commission should provide all actors with t he legislative clarity and should enhance cooperation with third countries.

Conclusions

Highlights of Johnson & Johnson's suggestions.

As we support the aim of the EU Commission to amend the legal framework for medicinal products in its effort to combat the counterfeiting of medicinal products, we would like to highlight some of the aforementioned suggestions that need immediate attention and appropriate action by the EU Commission:

- Direct and immediate ban of repackaging, except under the control of t he Marketing Authorisation holder or their designee;
- Less complex and more transparent supply chain / Facilitate 'direct' distribution practices;
- Introduce a harmonized inspection system in the EU;
- Require tamper evident packaging to be implemented for all prescribed medicinal products;
- Mass serialization to be implemented in three phases;
- Selection of serialization codes, data standards and data carriers to be made with global harmonization in mind.

Johnson & Johnson's suggestions for further actions to address the problem of Counterfeit medicinal products within the EU:

We acknowledge that this Consultation is a significant start in addressing the key elements of the counterfeit framework policy; nevertheless, we maintain that more actions are needed t o address the issue effectively within EU:

- Zero-tolerance public policy that helps eliminate counterfeiting by encouraging:
  - Laws that make it easier to prosecute counterfeiters;
  - Greater penalties for counterfeiters;
  - Increased resources for law enforcemen t and Customs activities;
  - Increased collaboration among governments and national and international law enforcement agencies;
- Actions taken to increase p ublic awarness about the risks associated with use of medicines bought from unauthorised sources (eg, I nternet pharmacies).
  - Establishing a surveillance program of both internet and supply chain activities to find and monitor potential counterfeiting operations;
  - Stringent legislation to manage healthcare products being offered for sale on the Internet.
- Mandatory for Competent Authorities to establish hotline(s) for Health care professionals and patients, to report suspected counterfeit medicines.
- Support for an increase of awareness and education for patients, business partners, healthcare professionals and consumers about counterfeit products and their roles in protecting individuals' health and in identifying and reporting counterfeits. We encourage increasing governmental and industry resources to this end.