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Consumer goods
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PREPARATION OF A LEGISLATIVE PROOPOSAL TO COMBAT COUNTERFEIT MEDICINES FOR HUMAN USE

SUMMARY OF RESPONSES TO THE PUBLIC CONSULTATION DOCUMENT

1. INTRODUCTION

In response to the public consultation on "Key ideas for better protection of patients against the risk of counterfeit medicines"[1], the Commission received 123 contributions from stakeholders. Of these, 100 were from industry (pharmaceutical industry, distributors, suppliers of active ingredients, consultants), 15 from citizens, patient (groups), and academics, and 8 from health professionals, pharmacists and health insurers.

4 stakeholders (Eli Lilly, Bayer Healthcare, SICPA and Thornton & Ross Ltd.) requested their entire submissions to be treated confidentially. The other stakeholder responses have been published on the "pharmaceuticals - website" of the European Commission.[2]

Of the 123 stakeholder contributions, in terms of regions, 20 contributions were received from EU-wide associations, 29 from Italy, 14 from the UK, 9 from Germany, 4 each from France and Switzerland, 3 each from Poland and Ireland, 2 each from Malta, Denmark, and the Netherlands, 1 each from Austria, Sweden and Spain, and 18 from non-European third countries. 10 stakeholder contributions were global associations or could not be attributed in terms of region.

30 national and regional authorities profited from this stakeholder-consultation to inform the Commission of their views on the matter.

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1 http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_03/consult_counterfeit_20080307.pdf

2 http://ec.europa.eu/enterprise/pharmaceuticals/counterf_par_trade/counterfeit_consult_2008.htm

2. GENERAL REMARKS

2.1. Relevance

The initiative was unanimously welcomed by virtually all respondents who stressed that urgent and decisive action was needed, and that the problem of counterfeit is increasing exponentially.

Some respondents considered that the known cases were just the "tip of the iceberg", as in particular wholesalers and manufacturers are not keen on being related to counterfeit by media and the public. They argued that the problem is larger than anticipated and that discovery of cases is often pure luck. While it was repeatedly stressed that the situation could lead to "disaster", very little quantified information on the extent of the problem was given. One respondent (a wholesaler association) estimated that counterfeit packs represent "probably less than 1%" in one Member State.

A few respondents reminded of the need to stay rational and evidence-based – in particular regarding the lawful supply chain. One respondent argued that there is not necessarily increase in *counterfeits*, but increase in *surveillance*, including in the lawful supply chain.

While some respondents stressed that health considerations override the interest to mitigate compliance costs, others warned of an increase in bureaucracy and administrative burden. In this respect, it was opined that changes should not lead to an overhaul of the existing legal systems (rather, adapting some technical provisions) and that implementation times should be sufficiently long.

Some contributions highlighted the need to avoid unharmonised approaches across the EU. Others recalled that increased costs may be passed on to patients in second-round effects.

Various respondents highlighted the costs of counterfeit for industry and stressed that companies have anti-counterfeit strategies in place. In this context, the question was raised why industry should bear costs of counterfeit, rather than the society as a whole (i.e. the taxpayer). It was highlighted that, today, costs for destruction of counterfeit and recall of these products are in practice borne by the trademark owner.

The link to organised crime was stressed by several respondents.

2.2. Causes of problem

Practically all respondents agreed with the Commission's assessment of the causes of the problem and welcomed the comprehensiveness of the analysis, in particular the inclusion of aspects of active pharmaceutical ingredients ("**API**") quality/authenticity.

In particular, all respondents supported a "joint approach" with a bundle of measures, i.e. the look at different aspects. It was highlighted that U.S. FDA is following the same "multi layer" approach.

Finally, there was nearly unanimity that enforcement is a crucial element in the fight against counterfeit. This should entail the recall of licenses for non-compliant firms, penal sanctions, tighter checks at the outer borders of the EU and better information-sharing of customs authorities.

2.3. Other aspects

The public consultation was taken as opportunity to point at other, sometimes related aspects, such as the definition of "qualified person" (arguing that this person should be a pharmacist), the GDP guidelines (requesting a modernisation), pharmacies as buying groups, direct supply strategies (arguing that they encourage alternative sourcing, incl. internet purchase), the differing pace in Member States of approval of variations, the requirements for the "responsible person" (concerning wholesaling) and the illegal diversion into the EU of products destined for third country markets under favourable price regimes.

Several respondents highlighted additional aspects outside the scope of pharmaceutical legislation. These included, for example, assisting third countries with weaker regulatory/enforcement structure and a strengthening of criminal law measures against counterfeiters.

Many respondents pointed at the risks stemming from the *unlawful* supply chain, in particular internet pharmacies not complying with the requirements in the respective EU Member State(s). Some respondents entered a discussion as to whether internet pharmacies should be subject to a specific Community regulation and how. Others recognised that the main problem lies with dubious internet pharmacies established in third countries which are *de facto* accessible for EU-patients from within the EU but not controllable by Member States.

Some submissions raised possible links with the ongoing files "information to patients" and "pharmacovigilance".

3. PRODUCT PROTECTION MEASURES AND PROHIBITION OF THEIR MANIPULATION

3.1. Safety features

3.1.1. Technology

Regarding the present system of batch numbers, there was widespread agreement that batch numbers do not efficiently contribute to the fight against counterfeit, as the number of units within a batch can be enlarged and the number be replaced easily.

On the other hand, the vast majority of respondents pointed out that it would be premature, ineffective and even counter-productive to "prescribe" in secondary legislation (i.e. in a Directive adopted by the European Parliament and the Council) a specific safety/authenticity feature for medicinal products. The multitude of techniques and the need for flexibility was highlighted. Some respondents argued that the choice of a technology should be left completely to the manufacturer

and that any technology has to be risk-adapted. Legislation should thus not be too prescriptive and further implementing legislation was needed.

On the other hand, several respondents stressed the importance to act quickly, as Member States are taking unilateral measures which would create considerable costs.

Finally, it was opined that any system would require thorough review after some years as well as a fall-back mechanism if it fails.

Turning to more concrete technologies, the following was observed:

3.1.1.1. Serialisation

There was almost unanimity that serialisation is in principle a useful technology to combat counterfeit. One respondent stressed that the tobacco industry is considering a similar technology.

On the other hand, the multiple technical and legal difficulties were highlighted. These would require a long period for implementation. The U.S. example shows this. Therefore, a stepwise approach (for example, first including certain high-risk products) would have to be considered (see below). On the other hand, some companies recalled that this approach would remove economies of scale.

Importantly, serialisation was highly supported by the research-based industry, but more critically assessed by the self medication and generics sector who argued that their products had not been targeted by counterfeiters in the past and that costly product protection measures for those products would not bring additional benefits to the patient. Wholesalers and pharmacies showed a rather positive reaction to the concept of serialisation. This is crucial, as serialisation requires the involvement of many different actors.

Concerning verification, it was highlighted that pharmacies may use serialisation to facilitate inventory management.

Consumers should have a possibility to verify serialisation numbers via the phone or the internet.

Many submissions highlighted the international developments for example in the U.S. (in particular California) and in Turkey arguing that now was the ideal moment to build up a global harmonised approach.

Some submissions highlighted the data protection and competition issues which serialisation would rise.

3.1.1.2. Pedigree

Pedigree is a record of past ownership and transaction of a batch.

There were conflicting voices on the effectiveness of a pedigree. While some considered it as useful tool to back-trace (referring, for example, to similar aspects in the fresh meat sector), others argued that a pedigree does not add much to fight counterfeit.

In any case, it was widely stressed that a pedigree is a very complex solution and can only be considered as long-term aim – in particular if the system was to be automated. The U.S. example shows that very long implementation time is needed in order to address technical and financial obstacles.

Moreover, the high costs, which would be particularly burdensome for OTC-producers and SME, were highlighted. Several respondents recalled that a pedigree may affect negatively the throughput in warehouses.

Moreover, competition concerns were raised. The question as to who would have access to the pedigree database was characterised as “crucial”.

It was stressed that, in any case, use should be made of existing standards, such as the GS1 standard.

3.1.1.3. Others, incl. seal

Many submissions discussed the feasibility, effectiveness and efficacy of a seal in any form. Some criticised the concept of a seal as overly simplistic or “naïve”, adding costs without increasing security. Others criticised that efficient seals can only be verified by experts and that they would give a wrong feeling of safety. It was also stressed that the place where the seal is affixed (i.e. the product itself, the inner or the outer packaging) was crucial: A situation should be avoided where one “tracks cardboard, not product”.

On the other hand, a multitude of different concepts were presented which allegedly render counterfeit either impossible or uneconomical. These techniques included digital signature by asymmetric cryptography, colour-shifting dosages, watermark technology, chemical markers, flavour or aroma-adding, individual dosage level, DNA-coding, NIR-spectroscopy, electronic features, excipients tag, etc., etc.

It was stressed that seals were nothing new in the pharma sector and common practice in the food-and-feed sector. It was also highlighted that, in practice, a blister is a simple seal and that bottles often bear a seal "per se".

Some respondents stressed the need to ensure that a layperson (e.g. a patient) can identify the seal. Others, on the contrary, stressed that this would give a false feeling of security and that covert seals are preferable. Some highlighted that a combination of various technologies was needed.

The possibility of temperature-sensitive seals was considered to address also shortcomings in the cooled supply chain.

3.1.2. Scope

Many respondents discussed the scope of a safety feature. The large majority of respondents highlighted that an "intelligent", risk-based approach was needed for determination of the scope. For example, certain product groups should be primarily considered, such as injectables, expensive or high-volume medicines, or biotech medicines (which typically do not have a taste or colour).

The generics and OTC-producer challenged the argument that OTC products are equally affected by the problem. It was also argued that vaccines should be excluded in view of their peculiar distribution regime. The possibility of a "step-wise approach" was considered.

On the other hand, some respondents stressed that a limited scope would lead to confusion and that it would not allow exploiting scale effects. Moreover, it was argued that counterfeiters are very flexible and that it was difficult and even unrealistic to forecast a risk profile. The example of pandemic flue shows that risk profiles can change rapidly.

3.2. Prohibition of manipulation of safety feature

This item of the public consultation sparked many differing reactions and was the only item where views were fundamentally opposed amongst different stakeholders.

Holders of the original marketing authorisation stressed that it was vital that safety features (such as serialisation number or seals) which are affixed on the packaging cannot be removed or changed subsequently. They stressed that any effort in this respect was futile if the safety feature can be subsequently manipulated. Moreover, without a sealed package, there was a risk that a fake product is introduced into an (original) pack.

Many respondents pointed at the impact for re-packaging practices in the EU. This would concern, for example, re-packaging to ensure availability in small markets.

Moreover, respondents highlighted that parallel traders have to re-package or at least open the outer packaging in order to comply with the language and packaging regimes in the destination country. In particular parallel traders criticised that this key idea had been lobbied by the research based industry and would essentially be an attempt of putting parallel traders out of business.

Parallel traders also questioned the link between counterfeit and parallel trade. They argued that counterfeiters have no interest to pass via parallel traders who may, in the course of the re-packaging, detect the counterfeit earlier than a wholesaler. In this respect it was argued that, in fact, parallel traders provide for an additional safety net.

It was also argued that *if* safety features are contained on the packaging, parallel traders should be allowed to reproduce them and to reaffix them or to add their own safety features. In response to this, it was stressed that it was not realistic to require an originator to share safety-technologies with the many potential parallel traders.

In view of the potential negative impact on parallel trade, several respondents, including health insurers and some Member States authorities, highlighted its important role in ensuring intra-brand price competition for patented medicines thus leading to savings for health insurers and/or the exchequer. It was also argued that parallel traders are important to ensure a sustainable wholesale of medicines.

It was also stressed that OTC patients often wish to read the leaflet before purchasing the product, that pharmacists need sometimes to open the pack and that the possibility for patients with arthritic fingers to open packs should not be impaired. Finally, it was stressed that re-packaging is required for clinical trials.[3]

4. DISTRIBUTION

4.1. General remarks

There was widespread agreement that today's distribution system constitutes a challenge in term of ensuring a counterfeit-free supply chain: There is a multitude of participants involved with an increasingly long distribution chain that changes often. In particular, the high number of interim traders ("brokers"), with little or no knowledge of the sector and the products was criticised. In this respect, several submissions stressed that "medicines supply is only as clean as its dirtiest link".

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[3] Note, however, that medicinal product for clinical trials are not within the scope of the Community Code for medicinal products (Article 3(3) Directive 2001/83/EC).

One interesting aspects, which had been raised by some respondents, was the idea to render reporting of counterfeit products obligatory for wholesalers.

4.2. Including more actors in scope of wholesalers

Against the background of these general comments, this measure was unanimously supported. The question focussed more on details and in particular on the question, which concrete actors should be included. In this context, distributors who only export, and brokers in third countries, were discussed.

Some cautioned that a definition would have to be carefully drafted (also in view of the translations in the different official languages) and that mere transporting companies should not be included. Moreover, "trade" (i.e. transactions) within a company should not be covered.

It was outlined that not all actors can be subject to the same obligations and that a classification system for the different degrees of involvement was needed, so that inspections are adapted to the different actors.

On a different matter, one respondent highlighted that GDP should include rules on procurement of medicines.

4.3. Strengthen inspections

Here too, the important role of enforcement was highlighted. In this respect it was emphasized that the adoption of GDP as Directive would have limited impact, as it is already satisfactorily implemented in the Member States.

It was stressed that a better cooperation was needed, including avoiding duplication, coordination by EMEA, coordination at international level and strengthened inspections in third countries.

There were many suggestion how to render inspections more targeted and how to support them from the perspective of the Community legislator: Points raised concerned inspections of customs warehouses, revised Compilation of Community Procedures on Inspections and Exchange of Information ("**CoCP**") addressing, albeit in a flexible manner, wholesalers, obligatory CoCP also in third states, sunset clauses for GDP licenses and the possibility to restrict certain medicines to certain wholesalers and *vice-versa*.

It was stressed that administrative costs have to be considered and that, already today, inspecting competent authorities are sometimes understaffed.

One submission stressed that wholesaler certificates should be better protected against counterfeit.

4.4. GDP Database

This idea, too, was almost unanimously welcome as it would facilitate verification and bring an end to today's practice where wholesale licenses are simply copied to support alleged compliance.

Comments focussed on practical matters, such as who manages the GDP database and feeds it with data.

One submission suggested including in the database results of audits.

5. "IMPORT FOR EXPORT"

Here too, there was widespread support for the assessment of the problem and the measures envisaged. Existing difficulties, in particular in view of the recent case-law of the European Court of Justice, have been highlighted.

It was stressed that the food sector is considerably more advanced in addressing the issue.

Respondents highlighted in particular the need to have clarity with regard to "free zones" from the perspective of pharmaceutical law and rules regarding the interactions with customs. "Import" and "transit" should be defined for the purpose of pharmaceutical legislation.

Concerning substantial requirement, several respondents highlighted that a full batch analysis was not necessary if the exporting country had a functioning regulatory and surveillance system.

Several respondents recalled that large companies import their own products for export. They argued that, as there is a pharmaceutical quality system, re-testing should not be required.

Some respondents recalled that in practice, today, certificates from third country authorities are requested for imported consignments.

The importance to ensure correct storage conditions in customs warehouses was highlighted.

6. ACTIVE PHARMACEUTICAL INGREDIENTS (API)

6.1. General remarks

Regarding safety and authenticity, virtually all but one submission confirmed that the concerns set out in the public consultation document were justified and that the issue of counterfeit must not be restricted to the finished product.[4]

While one submission highlighted the need to also consider excipients, another submission called for an *ex*clusion of herbal substances from this debate.

[4] To characterise further the large approach, some submissions suggested referring to "rogue API", rather than "counterfeit API".

6.2. API and enforcement, in particular in third countries

The unanimous view of the respondents was that Community provisions ensuring efficient enforcement are too weak, in particular with view to third country manufacturers. It was highlighted that, at present, the only very few Member States inspect outside the EU (these inspect approx. 20 plants per year).

With regard to checks by third country authorities it was argued that these work often with lower standards – in particular concerning exported substances. It was stressed that this situation has created a non-level playing field. One respondent estimated that a manufacturer who is Good manufacturing practices ("**GMP**") non-compliant saves approx. 25% of production costs. This situation is aggravated by strong competition in the active substances industry as well in the field of generic medicines.

Some contributions argued that imports of API from countries with lower GMP standards should be banned and called for more aggressive and stronger enforcement. EMEA should get involved in inspections through coordination of work-sharing programs amongst Member States authorities. One submission contemplated a "European inspections team" for API. Moreover, duplication of controls by reliable third country inspections should be avoided and cooperation strengthened. This was particular relevant as inspections in third countries is not easily feasible for small Member States.

With regard of the quality of inspections, it was highlighted that these have to focus more on counterfeit aspects and that they should be based on a physical visit of the plant, rather than a check of documentation.

There were different appraisals of the contribution of GMP to combat counterfeit. Some considered GMP as "crucial". They argued that – while GMP-non-compliance does not make a product a counterfeit - counterfeit API are usually also severely GMP non-compliant. On the other hand, one submission argued that impaired quality has nothing to do with counterfeit.

Against the general claim of better enforcement, some respondents cautioned that manufacturer of medicinal products should continue to be held primarily responsible.

One respondent suggested that labelling of a medicinal product should include information on API.

More specifically, on authorisation and notification requirements the following was raised:

- Authorisation obligation: Many respondents did not explicitly address this point. Those who did supported an authorisation obligation in particular for third country manufacturer. This would lead to obligatory inspections rather than on inspections based on suspected "non-compliance".

- Notification obligation: Most respondents supported this point, highlighting that France has already introduced notification requirement for importers

and distributors. Also, Italy is going to strengthen unilaterally its rules as of 1 January 2009. While respondents supported inclusion of distributors in the notification requirement, they spoke against a notification of each imported consignment.

6.3. Audits

Most respondents confirmed that audit is a very useful tool to increase compliance and to avoid "back-to-back" business. Only one respondent disagreed stressing that audits did not give an insight in the actual production process.

Some submissions reminded that auditors may be influenced by economical considerations. To address this, audits should be done by independent, qualified personal and Member State authorities should be somehow involved in the audit, for example through certification or accreditation.

Some submissions requested clear guidance as to the content of the audit and qualification of the auditor, while others stressed the need to maintain a flexible system, in particular concerning the frequency of audits.

A few submissions pointed at practical difficulties, such as access to the closed part of the drug master file. It was also stressed that the audited should agree to the audit.

It was highlighted that, currently, shared third-party audits are not very common. In order not to increase costs (in particular for SME), duplications of audits should be avoided, and an "audit database" was suggested.

One respondent stressed that package producers should be audited too.

6.4. Other aspects

Many respondents commented on the key idea, put forward in the public consultation paper, to apply "fingerprint techniques" in order to check the authenticity of the product. While this idea was in principle welcome, several submissions cautioned that it could not replace good process and supplier control. It was also stressed that technology evolves fast and that no definite technique should be fixed in Community legislation.

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