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.

Record of the Detailed Comments

Comments regarding question
1. Do you think that the problem of counterfeit medicines is well addressed in the EU Commission proposal?

In Part, but I would propose the following amendments/changes:

- It is well addressed but I feel that there is a hidden agenda to target the demise of Parallel imported products across Europe by not allowing secondary packaging to be opened for PIL changing by licensed GMP repackaging plants. NIR technology should be given the green light as routine testing in combating counterfeit medicines.

- Internet trading of prescription medicines should be strictly prohibited within the EU.

- Internet supplies have to be monitored.

- The proposal is too far reaching. The burden on the Q-systems is further increasing. Manufacturers of counterfeits will find new holes in the net, the profit margins are too attractive. On the other hand more stringent rules could be a good piece of protectionism for European API– and drug manufacturers.

- It is addressed quite well but the need for co–operation with customs and police should be emphasised. Counterfeit is not (only) a GMP issue but a criminal activity.

- Would question if the area of parallel importation needs to be looked at and the rules and regulations governing this area.

- The role and responsibilities of the regulators and the industry need to be clearly defined. Also if the GDP certificate is to be viable and trustworthy the mechanism of implementation and control has to be clearly defined. Also the pack traceability concept is excellent but will take the industry years (if ever) to implement through art work changes!! California has just suspended a state requirement for pack codes to 2 years as it isn't possible to do in the time.

- Parallel importation legislation and the weakness of enforcement on PI manufacturers and Wholesale dealers has permitted counterfeit to get a hold in an otherwise highly regulated industry. The internet hasn't helped.

- Finished products manufacturers are responsible for auditing of APIs manufacturers. Both sides are overloaded with work and costs connected with this obligation. What shall be mandatory, are the inspections performed at APIs manufacturers sites (sort of pre–approval inspection).

- Use of Risk–Management (ICHQ9) approach for the entire supply chain to determine frequency of audits/inspections.

- An anti counterfeit approach should exist of 2 important aspects: supply chain as direct as possible and secondly unique id of each pack in combination with verification check at the level of retail.

- Again a broad brush approach; the risk with OTC products and non-synthesised APIs is less. The proposals do not take this into account.

- Audits/inspections of API manufacturers should be performed first of all by competent authority members. This because more doors will be opened for competent authorities and the reason for this upcoming desaster was brought on by the EU legislation.

- Set standards of supplier audit and encourage openness of reports to Reg authorities and manufacturers alike.

- 1. CEP holders should be subject to regular or compulsory audits.
  2. EudraGMP database with open access.
  3. When inspection reports or GMP certificates issued by EEA, MRA partners or other recognised authorities are available, these should satisfy statutory obligations of the MAH.

- It should clarify the obligations and responsibilities of brokers, traders and agents. This should have at least the same responsibility that the holder regarding the distribution of medicinal products, even API. As well as the Health Authorities should provide them the GDP certificate after a formal inspection.

Comments regarding question
2. Are the responsibilities as well as the task to be fulfilled by the Qualified Persons correctly addressed?

In Part, but I would propose the following amendments/changes:

- It is not correct to impose additional responsibilities to the QP while some governments (e.g. Germany) are boosting the possibilities to spread counterfeit medicines by prompting internet trade of medicines.

- It should be emphasised by our organisation that assuring the compliance with the new proposed regulations is not a part of the QP's legal duties but should be assured within the pharmaceutical manufacturer's Quality System. Qualifications of auditor must not be identical with those of a QP!

- What is a qualified auditor? And can this be a QP or is this someone from the authorities? So far the releasing QP is responsible for auditing API sources, will this stay like this or will shift this responsibility to the competent authorities?

- Task and obligations addressed to the QP are very ambitious. Without collaboration/help with Regulatory authorities probably it could not be fulfilled correctly.

- The responsibilities of the QP's are not clearly addressed. Furthermore, there should be clear requirements and qualifications for the QPs working in wholesalers who should take the responsibility of the GMP/GDP compliance.

- It is not clear at this stage of the key ideas collection who has responsibility within the supply chain.

- It needs to be clarified how far back in to the supply chain the QP needs to look for a supplier – there may be cases where going back tot he original manufacturer becomes effectively impossible;

- The reference to the QP is only made with respect to auditor qualifications!! This is a serious omission and needs to be rectified.

- QP primary directive applies for all cases. I totally disagree with the EU concept of QP declaration on the API GMP. It belies a complete misunderstanding of the issues it intends to address and certainly is not based on Quality Principles.

- Require APIs to be released by a QP and reinforce the responsibilities of the QP who is dispositioning the Drug Product with a more substantial contract between the API and DP QP's, even if within the same company

- For counterfeit medicines the QP could not only be responsible. The legislative of the community has to challenge the distribution channels. (internet and others)

- I think this position will generate some problem to the manufacturer of medicines but is a guarantee for the EU API manufacturers

- clear expectations required

- There are commercial and legal responsibilities outside of the QP responsibilities which need to be addressed. Placing the onus onto QPs is unrealistic as there are usually wider business considerations which impact upon the QPs ability to make decisions.

- The role of QP of DP manufactured is only mentioned for having the responsibility to assure that the API manufacturer comply the GMP.
  The role of the Holder QP in case of distribution chain should be defined, not all the companies ask to QP for defined the flow chart of distribution. I wonder how the QP can assure the GDP when a distribution centre is used for the distribution and then this use local wholesaler to send the product to the final user. Is the solution that the holder QP do audits? Or maybe could the solution be that the Heath Authorities is each country authorize appropriately all the distribution centre and wholesalers?

Comments regarding question
3. Do you support EMEA's idea to regulate products imported for the purpose for exportation as stringent as products imported to be placed on the Community market?

- Each country or region has its own regulation system. Why should the EU regulation be applied to regions outside EC?

- As a measure to prevent counterfeiting globally, this is probably well reasoned. But otherwise it is unnecessary.

- Ad IV.a: Records should be accessible without additional costs. If costs arise, the should be spread over all batches of an API or product.
  Ad V: wholesalers should be inspected as any other company that is bound to GxP rules.
  Ad I.b: audits of suppliers and wholesalers should be mandatory anyway, not only in case of suspicion of non–compliance

- Made in or delivered from the EU should have the same level of quality

- Absolutely. Quality MUST be market independent.

- I believe the regulation should be targeted against counterfeit which is a criminal activity. EU legislation is part based on re–testing quality assurance into a material, which is contrary to fundamental quality principles...and very expensive.

- Because of the possibility of parallel importation.

- Because products coming from EU should be considered safe. Transfer into EU should not be misused to mislead customers around its safety.

- There has to be an equivalent level of quality and safety for medicinal products.

- By allowing from a tacx pont of view the separation of the financial flow from the physical flow of the goods, and the fact that the QP is responsible for the quality of the goods, I find it only the logical consequence that the legal requirements on importing become as stringent as proposed.

- Please note the receipt of the European directive in Italy, decree 219 and amendments give as mandatory the authorization to import API from extra cee countries. The import from European Countries is under the evaluation of cGMP released by the agencies.

- This regulation helps us, also, the countries outside of Community market.

- In my opinion, it is needed to prohibit the re–pack or re–labelling any medicinal product or API if the brokers are not authorized by the local Health Authority. In case of any modification respect to the initial release of the product, who is responsible to assure the quality? it does not have any sense that the initial QP or Responsible Person have the responsibility of the final use of the product. It has been manipulated during the distribution chain.

Comments regarding question
4.*Do you think that a system for mandatory GMP inspections at API manufacturers by EU* Authorities (in the EU and outside of the EU) should be established?

- Current system places an intolerable burden on both API producers, and on drug product manufacturers, and leads to inconsistent approach

- This kind of inspection is more constraining that the audit performed by manufacturer. This is mainly the case when there is only one API manufacturer in the regulatory files.
- It will improve patients safety by zero, but add additional costs and reduce flexibility
- Inspections should be conducted by National or EU authorities and it should be discussed, whether audit reports of non EU Member States being members of PIC/S may be acceptable.
- This would be too slow and too costly
- Will be difficult – costs, timing ...
- I highly appreciate that the EU authorities have volunteered to perform these inspections and that the responsibility for the audits is not placed with the manufacturer.
- Manufacturers in the EU have to submit to inspections. The same rules should apply to those whose products (e.g. APIs) are imported into EU.
- Together with i.e. MRA countries and FDA. This is a global issue. Why not to try solve it globally by accepting GMP inspections of some non EU Authorities also? European Commission SHOULD EVALUATE what non–EU authorities or other bodies (i.e. EDQM, WHO) could be accepted for that. This is the only transparent way to ensure GMP globally.
- This is the responsibility of the manufacturer, however EU Authorities should have the right to do so but not mandatory.
- Should be in the responsibility of industry.
- I think this is not feasible and could be overcome by audits from other trusted national control authorities, e.g. in the light of a MRA
- It is quite clear that the QP has the ultimate responsibility for assuring quality of materials that are incorporated into products. Therefore it is the industry's responsibility to perform due diligence. In any event this would be an impossible task for the current state of EMEA or any other member state to undertake. The FDA acknowledges that they have only audited 7% of overseas suppliers.
- Qualification of auditors should not again become a closed shop for pharmacists as unfortunately is QP–qualification; what will be the legal accountability of the auditors? Is the QP still accountable?
- Yes, in accordance with the current TGA regulations. I.e. accepts MRA country audits + FDA. And they should replace mandatory audits.
- The burden is intolerable, both for generic manufacturers, and the API producers, who are facing multiple audits of the same product to varying standards. I have been told I will have to wait 3 years to audit one manufacturer – they are booked solid!!! The GMP inspector was not impressed, not accepted as an excuse.

- Focus should be outside the EU and the US. Unannounced inspections are problematic.
- Based on Risk.
- Government want less civil servants. The workload for these people is quite heavy already. Therefore an international collaboration and mutual recognition is a more efficient way to solve the issue. Joint training of national inspectors could be one approach. Third party audits could be also a possibility but here it will take to build up trust.
- Who will do the inspections? Does this still fall on the shoulders of the QPs or is it for the EU Authorities, this is not clear to me.
- This would be helpful but only if the obligation of the MAH for inspection would be cancelled and a official database is created according the CEP System.
- It will answer to a lot of questions a QP has in mind when he has to release a product.
- It should be appreciated a rules of QP of the manufacturer that imports the API in the evaluation, according to ECA rules of the cGMP compliance of the API manufacturer.
- A regular system for the GMP inspection at API manufacturers to be performed by EU Authorities must be established. The GMP report should be available for the finish product manufacturer as the FDA inspection reports.
- The issue of "atypical actives" e.g. castor oil, glycerin be resolved.
- Could such an audit be really efficient? It should be manufacturer's responsibility to assure the API of the high quality. The inspection can not prevent purchasing an API from other, non–audited sources.
- Very important.
- GMP–inspections by EU Authorities would probably be a good measure, but it depends on how this idea will be implemented. There are a great number of API manufacturers (especially in the Asian area) and it will take much time to inspect (most of) them. There have to be interim regulations for API manufacturers as well as the buyers in EU to prevent possible supply shortfalls, if the inspection should become mandatory.
- We believe EU authorities could make more effective use of resources by the registration, control & monitoring of auditors using improved audit guidelines and, in particular, third party auditors.
- Common database.
- Yes, absolutely but no only for sterile API or API from biological source. The GMP should be done at all API manufacturers. As it is a lot of work, the authorities should put more effort to establish MRA as much countries as possible.

Comments regarding question
5. Do you think that the various initiatives (European Commission, EQQM, WHO, OECD, FDA) are coordinated in a sufficient way?

- A global, public access GMP data base, with inputs from all official inspections would be useful
- I don't have a sufficient visibility on all those initiatives to give a documented opinion.
- It is certainly good to have actions on different levels. May be some more coordination could be helpful
- In order to really improve the global GMP atmosphere there should be common mutual recognition on GMP inspections between these parties. A common GMP inspection program would avoid duplicate work and ensure the best efficacy.
- I think that in this moment doesn't exist a good coordination between various initiatives. A lot of Asian suppliers are insufficient conditions to produce any raw material or drug product, but are agreed by a part of authorities. In same time is very difficult to evaluate the condition of storage and transport before receiving (for excipient with a large percentage in formulation: ex lactose or starch) Maybe the GMP rules will be enforced for foods suppliers and cosmetics suppliers equally for API suppliers , will be better . Maybe if for imported foods, cosmetics, drugs and raw materials will be increased the level of quality (in standard specifications) the counterfeits and poor qualities will be stopped.
- Responsibilities not yet defined appropriately
- There is no coordination that I would be aware of, just parallel action based on recent events
- If they are then it is ineffective! The EMEA document is in some ways a political 'knee jerk' reaction to the evolving situation particularly triggered by heparin and a global problem needs a global solution. EMEA & FDA collaboration is essential as a minimum. WHO should be included but is even more bureaucratically burdened than the other two. Having said that WHO is really the only reasonable voice for the third world.
- Probably not; but do not know the other initiatives.
- There is no co–ordination.
- EU and FDA shall finally join their efforts to exchange inspection results and accept mutual recognition.
- But, a working party of all interested organisations should be established as a sub–group to work with the EMEA.
- The issue is the various level of implementation in the EU member states.
- It always can be better but sometimes it depends on interests
- But I do not see a better way...

- I do not know the various initiatives.
- Because at the moment the positions of the EU countries are different. Italy approach is the inspection of API manufacturer for the Italian site and also for the Extra Cee countries.
- The FDA initiatives are more detailed. It would be a good idea to harmonize them.
- I do not know well all these initiatives but a think must be coordinated / harmonized.
- It always can be better....
- Despite best endeavours there is still a large variation in standards and interpretation between the various bodies.
- Better information exchange is needed, as well as harmonization of the regulations.
- I'm not sure, if I have a complete overview of all activities; however, an effective cooperation is necessary.
- To be honest, I do not know.