**THIS CONTRIBUTION TO THE EC CONCEPT PAPER CAN BE MADE PUBLICALLY AVAILABLE**

## Re : Assessment of the European Commission Concept Paper issued on 7th December, 2011, on the Implementing Act on the Requirements for the Assessment of the Regulatory Framework applicable to the manufacturing of active substances of medicinal products for human use

**General Considerations**

In order for the Falsified Medicines Directive (FMD) and this planned, related Implementing Act to be acceptable to our members, there are two very important conditions that **both** need to be met at the very minimum:

1. Assessment of Third Country Equivalence (TCE) should focus fully on the manufacture of APIs exported or to be exported to the EU. This should always be explicitly clarified for all items in any yet-to-be issued documents in order to avoid that assessment will erroneously be focused on APIs for domestic consumption only or on APIs destined for exportation to other regions only (such as the USA, Japan).

2. The term "APIs exported to the EU" should include both APIs *per se* exported to the EU and APIs exported to the EU as constituents of finished or semi-finished dosage forms. We are aware that, to our dismay, the current interpretation by the Commission excludes the latter category. This Concept Paper offers us the opportunity to reiterate forcefully that the Commission's interpretation should be amended to include the latter category and that such correction of the interpretation should be communicated through an as soon as possible to be issued official "Commission Communication".

The above two aspects are, respectively, very insufficiently emphasized / clarified (point 1 above) and entirely missing (point 2 above). Our main comments focus on these crucial points.

Already in the Introduction Section on page 2, our points 1 and 2 above should be explicitly stated and emphasized. By adding this in a clear manner to the Introduction will make it possible to refer back to it within each of the other sections of the Concept Paper. We, therefore, propose to add the following section to the Introduction:

***"The equivalence assessment process should be entirely focused on the manufacture of APIs destined to be exported to the EU from the yet-to-be assessed third country. This should include both APIs per se exported to the EU and APIs included within finished or semi-finished dosage forms (medicinal products) exported to the EU.***

***Manufacture of APIs destined for domestic consumption by patients in the exporting country or of APIs destined for exportation to non-EU regions or countries, should be excluded from the scope of the assessment"***

**Considerations per Consultation Item**

Consultation item n°1:

The major concerns are that point 1 above is not emphasized at all and point 2 above is entirely lacking. We propose that the above bold section be added to the Introduction Section and should be referred to here.

Consultation item n°2:

- Same comment as on Consultation item n°1.

Consultation item n°3:

- Same comment as on Consultation item n°1.

Consultation item n°4:

- Same comment as on Consultation item n°1. In addition, we believe that the following aspects are a reason for serious concern:

- Section 4.1 point 18 suggests that a review of relevant documentation may be one of the acceptable approaches for equivalence assessment. This option should either not be used at all or at most in highly exceptional cases when the third country has already very convincingly proven its equivalence with regards to exported APIs, namely by an already established Mutual Recognition Agreement with the EU that includes APIs. In fact, the latter approach is already implicitly included in the second bullet point of point 18. By no means should such an approach be deemed acceptable for the assessment of (major) API exporting countries, for example, China and India, as both have a history of serious safety incidents with exported medicinal products and pharmaceutical ingredients.

- It should be confirmed in a crystal clear, unambiguous manner that Section 4.3 point 21 refers only to situations of re-assessment of countries that have first undergone a successful equivalence assessment and have subsequently been included in the list of equivalent countries. Under no circumstances should any countries be included in that list without a thorough equivalence assessment, only to undergo assessment/verification three years thereafter. Probably this point is already clear in the Paper but we would like to see this very important point re-emphasised.

Consultation item n°5:

It should be clarified and emphasised that API manufacture in countries not included in the list of equivalent countries should be regarded as high risk, top priority for on-site inspections by the inspectorates of EU Member States.

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