Dear Mr Rossignol

We are happy to provide below the comments and suggestions of the CMC Regulatory Group of the Global Innovative R&D Division of Teva, referring to the public consultation paper relating to "Better regulation on pharmaceuticals: towards a simpler, clearer and more flexible framework on variations", Version 24 October 2007.

Summarized hereunder are our comments and suggestions:

The fact that the EC has announced its intention to make a simpler, clearer and more flexible regulatory framework on changes to medicinal products is very welcome. However, as this will necessitate changing the legal basis covering the changes to all marketing authorizations (centralized, decentralized/mutual recognition, purely national) and the regulations, we understand that this "worksharing" project will be a very lengthy process.
We suggest that the working procedure on this paper be expedited by adopting a graduated approach as per which:

a. The current annex (variation guideline) should be amended, as early as possible (during a transitional period) to enable, as suggested in "Better Regulation of Pharmaceuticals: Towards a Simpler, Clearer and More Flexible Framework on Variations" Version 20 October 2006 :
- downgrading of certain type IB variation applications to type IA
- annual reporting of type IA changes (except those subject to immediate notification)

b. A procedure for submission of annual reports should be established (for type IA changes and other minor changes).
In handling annual reports we consider the categorization of the type IA changes reported within it to be unnecessary/ redundant. We think there should not be a submission of separate type IA application forms as part of an Annual Report. We believe that it would be appropriate and sufficient to clarify at the beginning of the Annual Report the list of changes and amended sections of the CTD.

c. A guideline detailing the variations that should be covered by type II as well as type IB applications should be established (addressing the worst case scenario), while the type IA procedure should be considered as the default (maybe not necessitating a type IA guidance document detailing the changes covered in it*).
* Alternatively, a type IA notification guideline might be appropriate, but it would need to cover also issues which are currently not addressed in the guidelines, and are minor in essence (e.g. editorial changes, etc..) or any change not covered by the type IB or type II guidance.

Please note that the legal aspects of the guideline were not taken into consideration, only practical aspects were addressed in order to facilitate current working procedures and ease agency - industry work burden.

We thank you for the opportunity that was given to us to comment on the paper.

We would like to wish you a Happy new Year!!

With My Best Regards,
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