Comments on the draft Variations Regulations

1. Inclusion of purely national authorizations in the draft is welcome since as a result the same rules shall apply to all procedures for authorization. The concept of "design space" in reference to some variations is interesting and acceptable. The proposal to specify conditions for classification of variations and operation of the procedures in guidelines rather than Annexes to the Regulation seems acceptable, since in view of Art. 6 of the draft such guidelines should be binding as their issuing by the Commission is mandated directly in the Regulation, but the opinion of the Commission`s legal service on the their legal status seems necessary.

2. **"Do and tell" procedure**
   The scope of variations eligible for this procedure should not lead to situations, in which the product on the market cannot be immediately identified and monitored, which will happen even with immediately notified variations and especially when such variations are grouped, because of time lapse between implementation and notification. The notion of "immediate notification" should be specified, e.g. in days since putting the changed product on the market. Draft Regulation does not address situation, in which the notification of variations is rejected by the competent authority and the variations have already been implemented. Art. 21 (1) provides only for the information and not decision on rejection and thus excludes the right of MAH to challenge the rejection in court. How and when will the implemented and then rejected variations be reversed ? It seems that the rejection of notified variations by the competent authority should be addressed specifically in the Regulation, taking into account that rejection is an act of will of the competent authority having direct impact on the rights of MAH, therefore it may not be a mere information. Conditions of reversal of rejected changes should be provided for, including rejection on formal grounds (incomplete documentation, lack of fee payment).

3. **Grouping of variations**
   Grouping of variations across several MAs does not seem acceptable at this time since it would in fact entail instituting several separate administrative proceedings based on one application and the question arises what would be the legal outcome of this procedure.
   Grouping of variations in one MA may be acceptable, but the question arises what happens when some of the variations are acceptable and others are not. Draft Regulation does not address this issue, at the NtA meeting in November 2007 the Commission presented the view that grouping of variations should result in "all or nothing" outcome, but neither the draft Regulation provides so nor there seems to be a rational and legal basis for such outcome, because grouped variations still continue to be separate variations. If the option "all or nothing" is to be accepted, with the understanding that it is MAHs decision to take the risk of rejection of all changes due to unacceptability of e.g one, then this option must be clearly provided for in the Regulation. Line extension should be excluded from grouping because of a different procedure of evaluation, inclusion of extension into a group would be also contradictory to Art. 23 of the draft.

4. **Worksharing – downgrading of the classification of variation**
   It should be noted that the concept of downgrading is not provided for in the draft Regulation and is presented only in the explanations of the legal text. Should this

concept be accepted it must be clearly stated in the Regulation and not in the guidelines, because of its legal effect on the subsequent action of competent authority. Serious doubts arise as to the rationale and legal basis of downgrading resulting from the opinion of EMEA, particularly when the legal status of this opinion is not provided for and it is doubtful if under the Regulation 726 EMEA is mandated to give such opinions on variations for products other than centrally authorized. Similar legal doubts relate to scientific recommendation on unforeseen variations by EMEA, as provided for in Art. 5 of the draft. Downgrading of line extension to Type II variation, in case the whole concept of downgrading is preserved is unacceptable due to reasons stated in point 3, last sentence.

Except centrally authorized products it is the national competent authorities which are competent to authorize the product on their market and therefore downgrading due to the EMEA`s opinion seems to contradict their competence and responsibilities in relation to national authorizations. In the explanation to the legal text there is no reference to a situation in which a Member State does not agree with the EMEA`s opinion rendered within worksharing scheme and resulting in downgrading or its scientific recommendation on unforeseen variations, which puts these opinions into a vacuum, if not accepted by a MS.

In general terms the concept of worksharing may be worth further consideration and development with the Reference Member State as coordinator for the nationally authorized products rather than EMEA or CMDh, which has no mandate for the proposed procedure and with no downgrading effect of the assessment. However, it is not clear how to use this procedure for nationally authorized products, whose SmPCs are not harmonized.

5. Transitional period

Proposed legislation will have a large impact on the national pharmaceutical legislation in Poland requiring an amendment of the Pharmaceutical Act by the Parliament and the change of the structure of the fee system for variations, therefore we propose a two-year period of vacatio legis for the Regulation.