AD HOC WORKING GROUP ON
VALIDATION ISSUES/NATIONAL REQUIREMENTS

COMMON GROUNDS SEEN FOR INVALIDATION/DELAYING DAY 0

September 2008

CMD(h) has set up a *Working Group on Validation issues/National requirements in MR/DC procedures* in order to achieve transparency about raised invalidation/delayed validation issues and consequently avoid procedural delays. The working group has defined the most common grounds for invalidation/delayed validation for variations[1] and applicants are encouraged to be more thorough when compiling the documentation before submission of the application.

- The application form is either incorrect and/or incomplete with necessary information missing:
  For example:
  - incorrect procedure number[2]
  - incorrect or missing CMSs
  - an original signature is absent
  - the name of the medicinal product is not the name approved
  - the MA number(s) is incorrect
  - more than one product/strength are included in the same application form
  - present/proposed is not filled in or incomplete
  - boxes about amended product information are not ticked off correctly (when applicable)
  - checklist according to the regulation is missing (for type IA or IB applications[LOD1])
  - Type II variation is incorrectly specified (e.g. in case of variation application concerning quality part "Other" has been marked instead of "Quality")

- Missing or incorrect fee.

- The application has not been submitted in all MS even though this has been declared in the dispatch list.

- Dispatch list not submitted.

- Misinterpretation of what *can* be applied for as consequential changes and what *should* be applied for as parallel variations.

[1] Guidance on dossier requirements are given in
- *Comission Regulation (EC) No 1084/2003 of 3 June 2003: http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2003_1084/reg_2003_1084_en.pdf*
- *Guideline on dossier requirements for type IA and type IB notifications (July 2006):* *http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-2/c/var_type_1a1b_guideline_06-2006.pdf*

[2] For example MRP variation number incorrect (e.g. XX/H/0100/001-002/IA/01),
Specific number for each strength/pharmaceutical form should be stated (e.g. XX/H/0100/001/IA/01 and XX/H/0100/002/IA/01).

- Several not consequential changes are applied for in one application (eg. Update of several CEP's, deletion of several manufacturers[3])

- Type IA/IB variations: The relevant conditions are not fulfilled (eq, condition: "The change relates only to standard immediate release oral pharmaceutical forms and to non-sterile liquid forms" is ticked for a semi-solid preparation for cutaneous application).

- The documentation package is incomplete with necessary information missing:
  For example:
  - national translations are missing (for type IA/IB notifications) both annotated and clean versions
  - references missing, expert statement missing (for type II variations)
  - environmental risk assessment or justification for absence missing (for type II variations with extension of indication)
  - updated product information is missing (when applicable) both annotated and clean versions
  - Letter of authorisation/Power of attorney not attached if the name and address of MAH contact is different from the one approved

- Product information in electronic format not submitted (when applicable)

- Insufficient number of copies submitted (cf. Notice to Applicants, Chapter 7).

[3] Cf. CMD(h) Questions and Answers for the submission of Variations according to commission regulation (EC) 1084/2003: http://www.hma.eu/120.html